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SURGERY

A Monthly Journal Devoted to the Art and Science of Surgery

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SURGERY

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Original Communications

SURGICAL TREATMENT OF SIGMOID DIVERTICULITIS

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DIVERTICULITIS of the colon is considered a comparatively rare disease.[2] It has been estimated that diverticulitis will require surgery in approximately one in 2,500 persons over 40 years of age.[3] However, in the past, surgery has usually been reserved for treatment of the complications, notably, perforation, obstruction, and fistula formation. As late as 1939, Brown[6] decried the long period of hospitalization and the high mortality rate associated with the surgical treatment of diverticulitis. He urged a determined effort to avoid surgery, but admitted that it was futile and dangerous to continue medical treatment after complications had developed. This surgical laissez-faire attitude has permeated medical teaching. The common practice has been to treat acute diverticulitis with a supportive medical regimen. If complications have developed, they have been treated by palliative surgical measures in the hope that the diverticulitis or its complications would not recur. Simple drainage of abscesses with or without a proximal colostomy has been the usual procedure. In case of obstruction or fistula formation, a diverting proximal colostomy has been advocated. After the bowel has been at rest for from three to twelve months, it has been customary to close the fistula and restore bowel continuity. Very little impetus has been given to surgical excision of the diseased segment of the bowel, despite a high morbidity and a high recurrence rate associated with measures other than resection.

This conservative attitude was advocated in the era prior to the advent of chemotherapy and antibiotics, improved anesthesia, and the use of blood and other supportive therapy which have decreased the mortality and morbidity rates of resections of the colon. The great progress made in recent years in the surgical treatment of carcinoma of the colon has been largely disregarded in the evaluation of the surgical treatment of diverticulitis.

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At present the principles of surgical resection of the colon are well standardized and allow a direct attack on carcinoma of the colon with low mortality and morbidity rates.[13] The incidence of carcinoma of the colon and the urgency for early complete eradication of the lesion have given impetus to the wide acceptance of resection as the treatment of choice. In contrast, diverticulitis is an inflammatory disease in which the indications for surgical intervention have been limited. This has made it difficult for most surgeons to accumulate enough experience with the disease to encourage them in adopting a policy of definitive surgery. However, the morbidity and mortality associated with this benign disease seem to indicate that a more aggressive surgical attitude is necessary with resection of the diseased segment as the ultimate goal.

There have been a few reports since 1941 emphasizing the morbidity and mortality associated with surgical procedures other than resection in the treatment of diverticulitis. Smithwick in 1942[11] reviewed the surgical management of sigmoid diverticulitis. Late results, one to fifteen years following surgery, for measures other than colostomy or resection were collected from the literature in ninety-eight cases.[4-6, 9, 11] Of these, 45.9 per cent of the patients were living and well, 33.7 per cent were living but not well, 8.2 per cent were dead from other causes, and 4 per cent were unknown. In seventy-eight patients followed one to fifteen years after a proximal colostomy without resection 62.8 per cent were living and well, 15.3 per cent were living and not well, 10.2 per cent were dead from other causes, and 2.6 per cent were unknown. The immediate mortality rate for these two groups was variable depending on the type of operation performed. It was 23.7 per cent for acute perforations, 9.3 per cent for abscesses, and 18.9 per cent for bladder fistulas. The late mortality was 8.2 per cent and 9 per cent in each group, respectively. However, late results for resections of the sigmoid indicated that this is more effective treatment. Of 109 patients[5, 6, 11] followed one to fifteen years, 76.1 per cent were living and well, 7.4 per cent were living and not well, the late mortality was 3.7 per cent, subsequent death from other causes 7.4 per cent, and unknown 5.4 per cent. These data were corroborated by a review of fifteen years' experience at the Massachusetts General Hospital[11] where the late results in forty-two patients followed seven months to fourteen years after surgical measures other than resection revealed 47.5 per cent were not well; 78.9 per cent of these required further surgery for persistent symptoms or recurrent disease, and 12.5 per cent subsequently died of their disease. However, the sigmoid was resected in thirty-three cases with two deaths, a mortality rate of 6.1 per cent. Late results in twenty-five patients followed an average of four and one-half years after resection revealed 84 per cent living and well, 12 per cent living and not well, 4 per cent unknown, and no late mortality.

Pemberton in 1947[13] reviewed the surgical management of diverticulitis of the sigmoid colon. The cases were divided into two groups, the first group comprising 245 patients treated from 1908 to 1940, inclusive, and the second group consisting of 144 patients treated surgically during the years 1941 through 1945. This study was undertaken to appraise the different surgical procedures

employed in the management of diverticulitis of the sigmoid and to determine the effect of modern chemotherapy. The immediate mortality rate for resection in 146 cases treated prior to 1941 was 16 per cent, in contrast to 2.7 per cent for resection in 111 cases subsequent to 1941. Of the patients undergoing a proximal colostomy with subsequent closure of the colostomy without resection, only one-third remained well. However, after resection, approximately 80 per cent were cured. The results from these two groups are striking because they indicate the decreased mortality and morbidity rates resulting from improvement in surgical management during the past ten years.

Boyden in 1950[16] reviewed the surgical treatment of thirty-eight patients covering a twenty-year period, from 1929 to 1949. Three right colectomies were performed for perforation of diverticula of the ascending colon and cecum. Thirty-two of thirty-five patients with diverticulitis of the sigmoid and rectosigmoid had resection of the involved segment. Twenty-five primary resections and seven resections after preliminary colostomies were included. There was no operative mortality and no late mortality. In addition, 95.6 per cent of patients with sigmoid resections followed one to sixteen years were living and well.

An additional reason for early excision of the diseased sigmoid is the difficulty in differentiating diverticulitis and carcinoma.[8, 12, 15, 22] Pemberton, in his review of 389 patients with diverticulitis, revealed that in roughly 25 per cent of the cases carcinoma could not be excluded by clinical methods of examination. The sigmoid is the most common site in the colon for carcinoma, the incidence being 54 per cent.[7] Moreover, diverticula occur most commonly in the sigmoid, the incidence being 75 per cent.[1] This relationship increases the frequency of diagnostic difficulty and increases the hazards of surgical procrastination. It does not imply that carcinoma is more likely to develop in a segment of bowel involved by diverticulitis or diverticulosis than it is in a segment of bowel not so involved.[20, 23] Rankin and Brown[2] support this contention with a review of 227 cases of diverticulitis in which carcinoma was encountered in only four instances, an incidence of 1.8 per cent. Diverticulitis was present in only four of 679 cases of carcinoma, or an incidence of 0.6 per cent. Recently, Rowe and Kallmar,[23] in an extensive review, found only sixty-two proved cases of carcinoma and diverticulitis existing simultaneously in the same segment of bowel. It is generally accepted that there is no causal relationship between diverticulitis and carcinoma, yet they are frequently indistinguishable clinically, and grossly at time of operation. Boyden reported three cases of suspected carcinoma in which successful resections were performed. The lesions appeared grossly malignant at operation, yet pathologic examination revealed no carcinoma. This experience is not an uncommon one. It emphasizes the difficulty in differentiating carcinoma and diverticulitis, but it also points out the feasibility of early successful resection of the diseased segment of colon.

These considerations have convinced us that resection of the diseased segment of the colon in diverticulitis can be accomplished with a low mortality rate and offers the greatest hope for a cure. Consequently a more definitive surgical approach has been adopted in the therapy of eleven consecutive cases

of severe and complicated diverticulitis treated since 1946 at this hospital. This is admittedly a small series and far too early a time for evaluation of late results. However, it is hoped that this report will give impetus to a re-evaluation of surgical therapy and will stimulate a more aggressive surgical attack.

CLINICAL DATA

Resection of the diseased segment of the colon with end-to-end anastomosis was carried out in ten of the eleven cases without a mortality. One patient had a diverting colostomy and drainage carried out for obstruction, perforation, and general peritonitis. He was awaiting resection when he died of a fulminating viral hepatitis. Of the remaining ten cases, there were six primary resections with end-to-end anastomosis without a previous or complementary diverting colostomy or cecostomy. Four patients were treated by resection and end-to-end anastomosis after an earlier diverting colostomy. The colostomies were closed later in all cases. No cecostomies were performed.

CASE 1.—T. W., a 56-year-old white man, entered the Veterans Administration Hospital with a three-week history of lower abdominal crampy pain, a 9 pound weight loss, and lower abdominal tenderness. Past history revealed occasional mild abdominal cramps associated with constipation and relieved by cathartics. Examination revealed an acutely ill patient with a temperature of 101° F. and a leukocytosis of 18,000. There was left lower quadrant tenderness and spasm with a large pelvic mass palpable by rectum. Sigmoidoscopy revealed a cobbled mucosa and obstruction 22 cm. from the anus. Barium enema revealed a constricted segment of sigmoid with a pericolic mass. A diagnosis of diverticulitis was made, but carcinoma of the sigmoid with abscess formation was strongly suspected. The acute symptoms subsided under conservative therapy with antibiotics and a low residue diet. After preoperative preparation with Sulfasuxidine and streptomycin, surgery was performed on the twenty-fourth hospital day. A firm sigmoid mass was attached to the cul-de-sac between the rectum and the bladder. Wide resection with end-to-end anastomosis was performed. The resected segment, 25 cm. long, displayed marked pericolic and colic fibrosis characteristic of chronic diverticulitis. The patient was discharged on the twentieth postoperative day and has remained well for twenty months.

CASE 2.—K. R., a 50-year-old white man, entered the Veterans Administration Hospital with crampy lower abdominal pain, tenesmus, and loose stools of two weeks' duration. Six years prior to entry, incision and drainage of a perforated sigmoid diverticulum was performed. Subsequently he remained well except for occasional mild lower abdominal cramps. Examination revealed an acutely ill patient with a temperature of 101° F., tenderness and spasm in the left lower quadrant, and a palpable pelvic mass by rectal examination. Sigmoidoscopy revealed angulation and edema 17 cm. from the anus. Barium enema revealed narrowing of the sigmoid, diverticulosis, and an inflammatory mass posterior to the sigmoid. All clinical signs of acute inflammation subsided under conservative therapy with antibiotics and a low residue diet. The patient was prepared with Sulfasuxidine and streptomycin prior to wide resection of the sigmoid and an end-to-end anastomosis on the twenty-fourth hospital day. The surgical specimen measured 20 cm. in length and revealed a large subserosal abscess with two perforated diverticula. However, there was a predominance of fibrosis involving the wall of the colon and the pericolic tissue. The postoperative course was uneventful with discharge on the tenth postoperative and thirty-fifth hospital day. The patient has remained well for eighteen months.

CASE 3.—J. O., a 57-year-old white man, entered the hospital with crampy abdominal pain, tenderness, and fever of one week's duration. For two years prior to entry the patient

had suffered recurrent attacks of crampy lower abdominal pain and tenesmus associated with nausea and vomiting. Physical examination revealed acute left lower quadrant tenderness and spasm, but no palpable mass. Rectal examination was negative. Sigmoidoscopy revealed angulation and obstruction in the rectosigmoid. Barium enema outlined a narrowed sigmoid with an irregular mucosa, diverticula, and sinus formation. Roentgenologic impression was diverticulitis with sinus formation. The clinical signs of acute inflammation subsided under treatment with antibiotics and a low residue diet. After preoperative preparation with Sulfasuxidine and streptomycin, wide resection of the sigmoid and rectosigmoid and end-to-end anastomosis were performed. The surgical specimen was a constricted segment measuring 30 cm. in length. There were multiple outpouchings from the mucosal surface to the serosa, and polypoid hyperplasia of the mucosa. However, there was marked fibrosis of the wall of the colon, a narrow distorted lumen, and severe chronic pericolitis. The postoperative course was uneventful with discharge on the twentieth postoperative and forty-second hospital day. The patient has remained well for eighteen months.

CASE 4.—J. G., a 61-year-old white man, entered the hospital with a two-month history of crampy lower abdominal pain, constipation not relieved by cathartics, and lower abdominal tenderness. Similar symptoms were experienced ten years earlier but disappeared after ten days. Examination revealed left lower quadrant tenderness without spasm. The temperature was 100° F. and the white blood count 14,000. A pelvic mass was palpable by rectal examination. Sigmoidoscopy revealed edema and obstruction 15 cm. from the anus. Barium enema outlined a stenotic sigmoid with diverticula and a pericolic mass. After conservative therapy with antibiotics and a low residue diet, the colon was prepared for surgery with Sulfasuxidine and streptomycin. Resection of the sigmoid with end-to-end anastomosis was carried out on the ninth hospital day. The resected segment measured 25 cm. in length. There was marked fibrosis of the colon and pericolic tissue with a chronic sinus tract and marked narrowing and distortion of the lumen. The postoperative course was complicated by dehiscence of the wound on the second postoperative day. The wound was resutured and the subsequent course was uneventful. The patient was discharged on the twenty-first postoperative day. He has remained well for sixteen months.

CASE 5.—P. L., a 57-year-old white man, entered the hospital with a two-week history of crampy lower abdominal pain, tenderness, nausea, and occasional loose stools. Five years earlier the patient had incision and drainage of an abscess following perforation of a sigmoid diverticulum. A residual sinus tract drained intermittently for one year before healing. Barium enema at this time revealed a narrowed sigmoid with diverticula. There were no significant symptoms prior to this admission. Examination revealed an acutely ill man with left lower quadrant tenderness, spasm, and a palpable mass. The temperature was 101° F. with a leukocytosis of 15,000. Rectal examination was negative. Sigmoidoscopy revealed angulation and edema 25 cm. from the anus. Barium enema outlined a stenotic segment of sigmoid which would not distend with barium. The mucosa was irregular with scattered small diverticula. The acute signs and symptoms subsided under conservative therapy with antibiotics and a low residue diet. After preparation of the patient with Sulfasuxidine and streptomycin, resection of the sigmoid with end-to-end anastomosis was performed on the seventeenth hospital day. The resected segment measured 14 cm. in length and revealed marked fibrosis of the colon and the pericolic tissue with diverticula. There was stenosis and distortion of the lumen. Recovery was uneventful with discharge on the fifteenth postoperative day. The patient has remained well for fourteen months.

CASE 6.—J. C., a 55-year-old white man, entered the Veterans Administration Hospital with severe left lower quadrant tenderness and crampy abdominal pain of twenty-four hours' duration. Past history revealed a similar attack one year earlier, diagnosed as acute diverticulitis with a pericolic mass. The symptoms subsided under supportive therapy. In the interim he followed a restricted low residue diet with a daily saline cathartic and had no significant symptoms. Examination revealed a dehydrated, acutely ill man with a tempera-

ture of 103° F. and a white blood count of 21,000. There was left lower quadrant tenderness and spasm without a palpable mass. Rectal examination was negative. Sigmoidoscopy was negative. Barium enema revealed diverticulitis of the sigmoid. The acute symptoms subsided promptly with antibiotics and low residue diet. After a course of Sulfasuxidine and streptomycin, resection of the sigmoid with end-to-end anastomosis was performed on the seventeenth hospital day. The resected segment measured 18 cm. in length and revealed serosal edema and marked fibrosis of the colon and pericolic tissue. The postoperative course was uneventful with discharge on the fourteenth postoperative day. The patient has remained well for nine months.

In résumé, these six patients were admitted with clinical signs and symptoms of acute inflammation and partial colonic obstruction. Sigmoidoscopy revealed positive findings suggestive of diverticulitis in five of the six cases. An unequivocal preoperative diagnosis of diverticulitis was made by barium enema in five of the six cases. However, in one case, differentiation between diverticulitis and carcinoma was impossible. In all cases, the signs and symptoms of acute inflammation subsided rapidly under supportive therapy with penicillin and streptomycin supplemented by parenteral fluids and a low residue diet. Definitive surgery could be carried out nine to twenty-four days after admission. In each case the patient was prepared for surgery with a five- to seven-day course of oral Sulfasuxidine supplemented by 1 Gm. of streptomycin orally twenty-four hours before surgery. A wide resection of the colon was performed with excision of the diseased segment and the redundant sigmoid. An open type of anastomosis of normal bowel was performed in the presence of a good blood supply and without tension. Two layers of fine interrupted sutures were used for the anastomoses. Fine interrupted chromic catgut sutures were used for the inner layer in four cases and fine silk in two cases. All six cases had fine interrupted silk mattress sutures for the seromuscular layer.

The resected segments revealed minimal acute inflammation, but a preponderance of chronic inflammation with colic and pericolic fibrosis. The chronic inflammation had distorted the bowel and produced angulation and stenosis of the lumen in each diseased segment.

One patient had dehiscence of his operative wound. This was the only postoperative complication. There were no deaths.

All of these patients made a complete recovery and were discharged ten to twenty-one days after surgery. The average total hospitalization was 38.4 days. All have remained well since discharge from the hospital. One patient has been seen nine months after surgery, one fourteen months, one sixteen months, and one twenty months, while two have been seen eighteen months after surgery.

The four patients treated with a first-stage colostomy reveal the problems of surgical management and the morbidity associated with complications of diverticulitis.

CASE 7.—J. M., a 53-year-old white man, entered the hospital with nausea, vomiting, and loose watery stools of ten days' duration. For six months prior to entry the patient had noticed irregular bowel habits with progressive enlargement of the abdomen. Physical examination revealed an acutely ill man with enormous distention of the abdomen. An in-

distinct pelvic mass was palpable by rectal examination. X-ray examination revealed huge distention of the colon and small bowel, with obstruction in the region of the sigmoid. An emergency transverse colostomy was performed on the day of admission.

Postoperative recovery was uneventful. Subsequent barium enema revealed a 10 cm. irregularly narrowed segment of the sigmoid with normal mucosa and small diverticula consistent with the findings of diverticulitis. Subsequently, the patient was discharged after fifty days of hospitalization to await subsidence of acute inflammation in the involved sigmoid. He returned seven months later for resection of the diseased segment of the sigmoid. Wide resection with end-to-end anastomosis was performed with the removal of a 17 cm. segment of colon. The resected segment revealed a thin film of fibrin covering the serosa of an angulated thickened colon. There was a firm mass of pericolic fibrosis sharply angulating the colon. The specimen revealed chronic diverticulitis and pericolitis. Preoperative recovery was not remarkable with discharge on the fourteenth postoperative and twenty-fourth hospital day. One month later he returned for evaluation; barium enema revealed a 1 cm. sinus tract at the line of anastomosis. Closure of the colostomy was deferred but was accomplished later at another hospital. He has remained well for forty-six months.

The proximal diverting colostomy was necessary and probably lifesaving in this case. However, there seems to be little value to the long period of waiting before resection was performed. With antibiotics and supportive therapy, resection could have been carried out three or four weeks after the colostomy. Usually, closure of the colostomy can be performed three or four weeks following resection. However, prior to closure, the line of anastomosis should be outlined by barium enema.

CASE 8.—F. A., a 47-year-old white man, entered the hospital in March, 1943, with signs and symptoms of acute sigmoid diverticulitis. He received supportive therapy for one week and was discharged. One week later he returned with an acute exacerbation of symptoms. There was tenderness and spasm in the left lower quadrant, fever, and leukocytosis. After admission it was noted that the patient passed gas through his urethra. Barium enema revealed a contracted segment of sigmoid diverticulitis and a sigmoidovesical fistula. During this admission, operation was carried out with division of the fistula and closure with chromic catgut. He was discharged after eighty-eight days of hospitalization. Three months later he returned with recurrence of the sigmoidovesical fistula. After supportive therapy and diagnostic procedures, a second laparotomy was performed with division and closure of the fistula. This hospitalization required 213 days. Seven months later the patient returned again with recurrence of the fistula. This time he received supportive therapy without surgery and was discharged after forty-five days of hospitalization. However, three months later, the patient returned for seventy-one days of hospitalization, during which time a sigmoid colostomy, just proximal to the diseased segment, was carried out.

From the time of his discharge in March, 1945, until February, 1949, he had a malfunctioning colostomy. However, when he returned to the hospital this time, resection of the sigmoid colon and end-to-end anastomosis were performed. The fistula had healed during the four-year period of colostomy life. Nevertheless, the operation was difficult, requiring wide resection of the colon with mobilization of the splenic flexure. The anastomosis was accomplished with some tension. Consequently a complementary diverting proximal colostomy was performed in the transverse colon. The resected segment measured 26 cm. The wall of the colon was thick and fibrotic. The lumen barely admitted a probe. A 3 cm. fibrous tract lined with mucosa represented the fistula. The postoperative course was uneventful with discharge after twenty-nine days of hospitalization. Six weeks later he returned for evaluation. Barium enema and sigmoidoscopy were not remarkable. Consequently, intraperitoneal end-to-end closure of the colostomy was performed. This hospitalization necessitated only twenty-three days. The patient has remained free of symptoms for thirty-two months.

This patient reveals the morbidity that may be associated with conservative therapy as well as the inherent hazards of ill-advised procedures. Closure of the fistula without resection of the diseased sigmoid was doomed to failure.[15] An early diverting colostomy followed by early resection of the sigmoid, excision of the fistula, closure of the bladder and either suprapubic cystostomy or urethral drainage[18] of the bladder would have been the treatment of choice. Closure of the colostomy could have been carried out three weeks after resection when barium enema revealed the integrity of the anastomosis and adequacy of the lumen. The sigmoid colostomy used in this case was mentioned only to condemn it.[21] It functioned poorly for four years, interfered with the mobilization of the sigmoid at the time of resection and anastomosis, and could not be used as a diverting colostomy after resection was accomplished. It is significant that prior to an orderly planned program with early excision of the sigmoid as the objective, this patient had experienced six years of disability and 424 days of hospitalization. However, after fifty-two hospital days and four months of disability, he was relieved of his disease and has remained well for thirty-two months.

CASE 9.—G. R., a 48-year-old white man, entered the hospital in May, 1946, with acute sigmoid diverticulitis, perforation, and general peritonitis. Emergency surgery was carried out with incision and drainage. The postoperative course was prolonged and complicated by a persistent fecal fistula at the site of drainage. One month after entry a proximal diverting transverse colostomy was carried out. There was subsequent slow healing of the fecal fistula. Barium enema revealed diverticula but no evidence of obstruction in the sigmoid. Consequently, closure of the transverse colostomy was performed. After 300 days of hospitalization, the patient was discharged. Two months after discharge, the patient returned with signs and symptoms of acute diverticulitis and partial obstruction. Conservative supportive therapy with antibiotics and a low residue diet resulted in complete subsidence of symptoms and discharge from the hospital. Five months following discharge the patient returned with another exacerbation of acute diverticulitis. A pelvic mass was palpable by rectal examination and sigmoidoscopy revealed edema and obstruction 10 cm. from the anus. Barium enema outlined a diseased segment of sigmoid colon and a jejunocolic fistula. A transverse colostomy was performed with prompt symptomatic improvement. He was discharged after forty-seven days of hospitalization. Two and one-half months later he returned for wide resection of the diseased sigmoid, excision of the fistula, closure of the jejunum, and end-to-end anastomosis. The 12 cm. resected segment revealed a minimum of edema and extensive fibrosis of the colon and pericolic tissue, with a perforated diverticulum and a sinus tract lined with granulation tissue. Postoperative recovery was uneventful and the patient was discharged after twenty-seven hospital days. Two months later, intraperitoneal closure of the colostomy was carried out during a twenty-seven day hospital period. He has remained well for thirty-two months.

This patient with perforation of a diverticulum and general peritonitis should have had diversion of the fecal stream by a proximal colostomy concomitant with drainage.[21] These procedures would have promoted more rapid subsidence of edema and relief of obstruction, would have limited peritoneal contamination, and would have reduced the incidence of a fecal fistula. A further criticism in this case was the closure of the colostomy without resection

of the diseased segment. Colostomy closure without resection was doomed to failure in over two-thirds of the cases in which it had been attempted.[17] The subsequent course of this patient revealed the inherent hazards of temporizing surgical measures. The use of antibiotics associated with a diverting colostomy probably reduced the hazards of early resection of the sigmoid and the fistula.[11] A resolute plan of treatment consisting of a transverse colostomy followed by a resection of the diseased segment and closure of the colostomy was carried out during 101 days of hospitalization. Prior to this course of action the patient had eighteen months of disability and 390 days of hospitalization.

CASE 10.—G. P., a 62-year-old white man, entered the hospital in September, 1950, with acute sigmoid diverticulitis, partial obstruction, and a sigmoidovesical fistula. After supportive therapy with antibiotics and fluid replacement, a transverse colostomy was performed. The postoperative course was complicated by excessive bleeding from the colostomy. Investigation revealed a markedly enlarged spleen, esophageal varices, and a persistent anemia and leukopenia. Liver function studies and liver biopsy revealed no significant liver pathology. Severe left upper quadrant pain several years prior to admission suggested splenic vein thrombosis. As a result of these studies, a splenectomy and splenorenal vein anastomosis were carried out two months after the diverting colostomy. The spleen weighed 1,825 Gm. and revealed a characteristic fibrocongestive splenomegaly with phlebosclerosis of the splenic vein. Prompt disappearance of the hypersplenic syndrome and esophageal varices occurred. Six weeks later, after progressive nutritional improvement, resection of the sigmoid, excision of the fistula, end-to-end sigmoid anastomosis, and a suprapubic cystostomy were performed. The resected segment measured 23 cm. There was extensive fibrosis of the colon and the pericolic tissue with numerous diverticula and a sinus tract lined with granulation tissue. Postoperative recovery was uneventful. One month later the colostomy was closed after a barium enema revealed satisfactory healing of the anastomosis. The patient has remained well for twelve months.

This patient presented compounded complications. However, he does illustrate the good results obtained by orderly procedures carried out with early resection of the diseased segment as the ultimate goal. The patient was completely relieved of the symptoms associated with hypersplenism as well as diverticulitis after 180 days of hospitalization.

These four patients requiring preliminary colostomy averaged 305.3 days of hospitalization which emphasizes the morbidity of diverticulitis with complications. This figure is in marked contrast to the 38.4 days' average for the six patients treated with early resection and end-to-end anastomosis without colostomy. Boyden[16] revealed that the duration of hospitalization in cases in which resection was performed without colostomy was less than one-half that following resection in which a transverse colostomy was performed preliminary to, or as an adjunct to, resection. He also noted the total duration of colostomy prior to closure varied from one to three months, the average being nine weeks. The colostomies in these four cases existed for widely varying periods prior to resection, forty-eight months, seven months, four months, and three months. Total duration until closure was fifty-three months, five months, six months and six and one-half months. Orderly planned surgery with early resection as the ultimate goal would have reduced the time interval prior to closure of the colostomies in these cases.

PATHOLOGY

Pathologic reports of all resected segments revealed the predominance of chronic inflammatory changes in the colon and the pericolic tissues. Diverticula were found in the ten resected segments and in the autopsy specimen of the one patient dying of viral hepatitis before resection. Each specimen revealed marked chronic changes in the wall of the sigmoid with marked fibrosis and narrowing of the lumen. Similar chronic inflammatory changes were found in the pericolic tissue in all specimens. Two patients showed associated edema of the subserosa with fresh fibrin over the serosa. Another patient revealed a large fresh subserosal abscess. Two perforations were present in one patient. A sinus tract was noted in six patients, an old abscess in one patient and polypoid hyperplasia of the mucosa in one patient. Shallow ulcerations were noted in two patients. The most significant finding was the low incidence of acute inflammation and the predominance of pericolic involvement. These observations suggest that the acute inflammation which is superimposed on the irreversible chronic inflammatory changes subsides rapidly with antibiotics, and the chronic inflammatory changes produce the distortion and stenosis so characteristic of the disease. Because of this rapid subsidence of the signs of acute inflammation, i.e., leukocytosis, fever, tenderness, and spasm in the six patients treated with antibiotics and supportive measures, and the minimal acute inflammatory changes in the microscopic sections, early extirpative surgery could be performed safely.

DISCUSSION

This series of eleven cases is too small to justify absolute conclusions concerning the surgical treatment of diverticulitis. However, these cases do emphasize the morbidity associated with the complications of diverticulitis and the futility of surgical measures short of adequate resection of the diseased segment. We believe that resection should be the ultimate goal in the surgical therapy of complications and that palliative surgical measures are indicated only to prepare the patient for resection.

There is no question that a large number of patients suffer mild attacks of sigmoid diverticulitis which respond readily to medical treatment and reveal no significant x-ray changes in the sigmoid. These patients are probably well controlled under medical supervision. However, we feel that a patient who suffers a severe attack of acute diverticulitis characterized by elevation of temperature, leukocytosis, tenderness, spasm, and positive x-ray findings has severe inflammation in the pericolic tissue and the colon wall, which are permanently and irreversibly damaged. The extent of this damage represents the degree of vulnerability to repeated attacks of diverticulitis and complications. These patients are best treated by early wide resection of the involved segment and the redundant sigmoid after the clinical signs of acute inflammation have subsided. Similar treatment is indicated for the patient with severe recurrent attacks of diverticulitis because of the irreversible chronic inflammatory changes predisposing to recurrent attacks and complications. To these indications for early

wide resection of the involved segment and redundant sigmoid should be added the occasional case in which the differentiation between carcinoma and diverticulitis cannot be made. This includes those patients with severe hemorrhage complicating the diverticulitis in whom carcinoma or polyp formation in the diseased segment should be strongly suspected.

Surgery should be directed not only toward the removal of the severely involved localized segment of colon, but also to wide resection of the redundant sigmoid with subsequent open anastomosis of normal bowel in the presence of a good blood supply and without tension. The length of the ten excised segments of colon in this series is interesting. They varied from 12 cm. in length to 30 cm. The average length was 20.6 cm. Smithwick[11] suggested that more extensive resections resulted in better end results. The average length of the resected segment reported by Smithwick was 13.6 cm. with 85 per cent of the resections being less than 15 cm. Boyden reported the average length in 31 resected segments was 14.5 cm. However, two segments measured 5 cm. One of these was the only failure in the group and the second was the only one in which primary resection with end-to-end anastomosis resulted in a fecal fistula. We believe that removal of the redundant sigmoid is important in preventing future stasis and subsequent inflammation in diverticula remaining after resection, because a straight tube that can empty readily is substituted for the redundant bowel in which stasis is prominent. Residual diverticula were present in all of our resected patients, yet there has been no recurrent diverticulitis. Complications of diverticulitis are not more severe because there is a more extensive process in the colon, but, rather, because there is a more serious and persistent process in a localized segment of the colon.[1]

The six patients receiving early resection without a preliminary diverting colostomy illustrate the advantages of early elective resection after preliminary treatment and bowel preparation. It is significant to note in this group that all had signs and symptoms of acute inflammation and partial sigmoid obstruction. It is also significant that three of the six patients gave histories of infrequent mild abdominal cramps prior to the onset of the severe attack leading to admission and early resection. Yet the pathology of the resected segments revealed a minimum of acute inflammation and a maximum of chronic inflammatory changes. These findings suggested that the acute inflammation in these cases subsided rapidly under treatment with sulfonamides, antibiotics, and low residue diet. The severity of the chronic inflammatory changes further suggested that the pathologic findings were irreversible and were more prominent than the symptoms suggested. The efficacy of antibiotics and chemotherapeutic agents for colon sterilization and the lack of complete obstruction in these six cases made diverting procedures unnecessary. However, the use of antibiotics cannot supplant sound surgical principles of anastomosis in the presence of a good blood supply and without tension. If these principles cannot be followed, then a proximal diverting colostomy is indicated. Open anastomosis has been

performed with interrupted sutures of fine chromic catgut for the inner layer and fine interrupted silk mattress sutures for the seromuscular layer.

However, in the treatment of complications of diverticulitis, such as perforation, obstruction, or fistula formation, a proximal diverting colostomy is usually indicated and may be lifesaving. It is entirely probable that in some cases of abscess formation without complete obstruction, or in some fistulas, colostomy is not necessary. However, in these cases, dissection is often difficult and the proximal diverting colostomy is a real aid in the preparation of the patient for surgery and in the performance of the resection. The antibiotics and chemotherapeutic agents tend to cause an early remission of acute inflammation so that resection can usually be employed within a few weeks after colostomy. This timing is especially important in cases in which carcinoma cannot be ruled out. Subsequent to resection, the colostomy can be closed after three weeks if a barium enema indicates complete healing of the suture line.

A proximal colostomy in diverticulitis should be performed in the right one-half of the transverse colon. One of our patients showed the difficulties associated with an ill-advised sigmoid colostomy. Furthermore a proximal colostomy in diverticulitis should be completely diverting. Smithwick[11] reported two of six cases of resection developed leakage at the anastomosis site when a preliminary or accompanying cecostomy was performed. The cecostomy does not adequately divert the fecal stream and should not be used. A simple loop colostomy of the right one-half of the transverse colon with complete division of the bowel has been the method employed. This is a simple procedure and completely diverts the fecal stream. For closure of the colostomy, an intraperitoneal procedure with an open end-to-end anastomosis is preferred.

The five cases of complications of diverticulitis exposed the morbidity associated with ill-advised procedures and temporizing or palliative measures. Their ultimate course of treatment revealed the efficiency and the benefits of planned procedures with resection as the ultimate goal. Incision and drainage of abscesses, closure of perforations, and diverting colostomies are all sound procedures for the treatment of complications. However, these procedures should be preliminary measures and should be followed by extirpation of the diseased colon. The mortality and morbidity rates are too high when a diverting colostomy is followed by closure of the colostomy without resection.

Complications offer a real challenge to the surgeon. Our experience and a review of the literature have resulted in our reformulating a few fundamental principles for the treatment of complications. For the patient with acute perforation, incision and drainage, closure of the perforation, and a proximal diverting colostomy should be performed; for abscess formation, incision and drainage and proximal diverting colostomy are indicated; in obstructive cases, a proximal diverting colostomy is necessary. Resection of the diseased segment and redundant sigmoid will follow the preliminary procedures in three to six weeks depending on the individual case. Intraperitoneal closure of the colostomy will

follow in approximately three weeks after barium enema proves the integrity of the suture line. It should be added that the complication of severe hemorrhage should be treated by an early primary resection after a search for other causes of bleeding has been made. Massive bleeding is not a common complication of diverticulitis. Consequently, bleeding should lead to a high degree of suspicion of carcinoma or polyp formation in the diseased segment.[23]

An obstructive type of resection is not advocated because the edema and thickening of the pericolic tissue makes mobilization difficult and wide resection of the redundant segment usually cannot be obtained. Also, that procedure is frequently associated with small bowel obstruction.[11]

The complications of fistula formation were revealed in the two cases of sigmoidovesical fistulas and the one case of jejunocolic fistula. These cases again revealed the fallacy of temporizing procedures without a direct attack on the diseased colon. The plan of treatment should consist of a diverting proximal colostomy, early resection of the colon with excision of the fistula, and later closure of the colostomy.[15, 19] Urethral catheter drainage seems to suffice after excision of a sigmoidovesical fistula,[18] although a suprapubic cystostomy was performed in our case. The primary disease process is in the colon, not the small bowel or the bladder. The surgical attack should be directed toward the complete removal of the diseased colon.

In the treatment of sigmoid diverticulitis, surgical resection of the involved colon seems to offer the greatest hope for a cure with the lowest mortality and morbidity rates. Consequently, the indications for surgical extirpation of the diseased colon should be enlarged.

CONCLUSIONS

1. Ten cases of diverticulitis of the sigmoid treated by wide resection of the diseased colon and end-to-end anastomosis without a mortality are reviewed.

2. Enlargement of the indications for surgical intervention in sigmoid diverticulitis is suggested.

3. Earlier surgical intervention is urged with wide resection of the diseased segment and the redundant sigmoid as the ultimate goal.

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VISCERAL METASTASES FROM CARCINOMA OF THE DISTAL COLON AND RECTUM

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AS THE horizon of pelvic surgery broadens to include extended resections and exenteration of pelvic viscera with ureteral transplantation, one might expect an increase of rather bizarre metastases from carcinoma of the distal colon and rectum. In former years, if a rectal growth had extended to encroach upon the integrity of a neighboring organ, or lymph nodes locally or distant were involved, the abdomen was closed or, in some quarters, a loop colostomy was performed. The patient usually died of bowel obstruction, sepsis, hemorrhage, malnutrition, uremia, and, for the most part, causes which were mainly local in nature. This was the era that impressed on the mind of the layman and physician alike the heinousness of a colostomy, an impression that has been difficult to erase.

In more recent times the pendulum has swung to more radical surgery at an earlier moment, that the patient might live out a lengthened span of life despite the misfortune that has befallen him. This has been made possible by the advent of antibiotics, better anesthesia, blood transfusions, an intelligent understanding of nutrition in preoperative and postoperative care, and, as a result, a bold philosophy on the part of both the colonic surgeon and patient. We have reached a point in our genesis where high ligation of the inferior mesenteric artery on the aorta is almost routine in order to eradicate regional node involvement.[4] Abdomino- and ileopelvic node dissection is now carried out in low-lying rectal lesions to check the advance of cancer spread.[24-26] In some cases surgical extirpation for carcinoma of the anus and low rectum is not complete without bilateral inguinal and femoral node dissection.[19, 31] In 1940, Appleby[2] instituted the pelvic exenteration procedure and reported his series in 1950. His results were impressive and encouraging, and many others have boldly accepted the operation to eradicate pelvic cancer.[11-15, 17] Other reports have gone further to include partial hepatectomy[20, 57] and even lobectomy[27, 52] in order that alleviation and palliation may add to the comfort of the patient. Wangensteen's "second look" method is still in its comparative infancy, the rationale being to remove any spread or recurrence prior to symptomatic notification.[59]

In spite of these surgical triumphs, many patients still die as a result of local cancer, but many more as a consequence of a metastasis in some remote recess of the body. This perhaps discouraging fact should not retard us in

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our efforts to remove every cancer whenever technically possible unless its advanced spread at the time of surgery dictates otherwise in our judgment. Once the tumor is removed, the patient's limited span is usually made more comfortable, and, indeed, he may even improve for a time in spite of existant metastases.

In order fully to appreciate the significance of visceral metastases from carcinoma of the distal colon and rectum, one should be familiar with the various modes of spread.

These cancers spread by direct extension, through lymphatic channels, and via the blood stream. The first two methods we can, in many instances, surgically challenge. The third is beyond our control but may be limited by the gentleness with which we handle the tumor before removal, as it is quite possible that cancer cells or an embolic fragment may be dislodged into the circulation by too vigorous manipulation.

It is not an uncommon incident at the time of laparotomy to discover the tumor adherent to the bladder, uterus, vagina, ovary, or small bowel. The problem immediately arises as to whether this attachment is inflammatory in nature or whether, in reality it is a malignant extension. Our decision most certainly influences the management of such a case. Structures adherent to colonic lesions should be resected with the tumor whenever possible, as malignant cells are often present at the point of contact. According to Sugarbaker,[53, 54] the degree of malignant involvement depends upon the extent of fixation. When the attachment was solid, the tumor invaded the bowel wall in 98.2 per cent of his cases and involved the adjacent structure in 40 per cent of cases. With lesser degrees of fixation these figures were somewhat modified.

The lymphatic spread of carcinoma is primarily embolic. Although Handley was an advocate of the permeation theory,[42] it has since been emphasized by Gilchrist that although this may also occur, the lymphatic spread of carcinoma of the colon and rectum is embolic.[34, 35] Jamieson and Dobson[45] found that nodes associated with a cancer fell into four main groups: epicolic, paracolic, intermediate, and principal. These groups tend to merge with one another. The epicolic and paracolic nodes are usually the first involved. It is usually not until these nodes are completely blocked that intermediate and principal nodes are involved by alternate routes. It has been demonstrated by Gilchrist[34] that the subcapsular space of a lymph node is involved first and that retrograde spread occurs only when these nodes are heavily laden with tumor.

We feel that venous spread bears an important relationship to the incidence of visceral metastases. Brown and Warren[16] have shown that 67 per cent of patients with intravascular invasion have visceral metastases. Although this mode of spread does not precede lymphatic spread, hepatic metastases are occasionally seen in cases where lymphatic spread has not yet occurred. Brown and Warren found blood vessel invasion in 61 per cent of their patients. Coller, Kay, and MacIntyre[21] found 15 per cent involved in vein invasion. Seefeld and Bargen[51] reported 20 per cent invasion of veins. Sun-

derland[55] stated 27 per cent of patients with carcinoma of the rectum have intravascular invasion. This mode of spread was found in 36 per cent of 75 specimens studied by Grinnell.[40]

From the various writings on this subject it has been concluded that the incidence of vein invasion varies directly with the histologic grading of Broders and the extent of spread according to Dukes. It has also been observed that low-lying lesions invade veins most frequently, thereby influencing the prognosis in an unfavorable manner. Anatomically the tumor emboli reach the liver via the portal system. From this site tumor cells reach the right heart via hepatic vein radicals and the inferior vena cava. Thence through the pulmonary artery, malignant foci may be set up in the lungs.

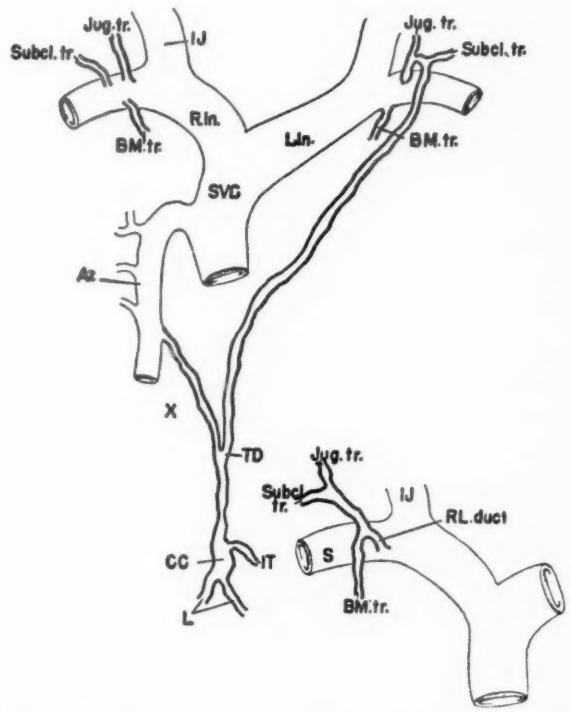

Fig. 1.—Main lymphatic ducts. Az, azygos vein; Jug. tr., jugular trunk; Subcl. tr., subclavin trunk; B.M. tr., bronchomediastinal trunk; CC, cisterna L, lumbar trunk; L.in., left innominate vein; R.in., right innominate vein; SVC superior vena cava; TD, thoracic duct; X, anastomosis between thoracic duct and azygos vein. (From Solnitzky, Othmar: Anatomical Factors Influencing the Spread of Cancer, Bull. Georgetown Univ. Med. Center 5: 176, 1950.)

When emboli pass through the pulmonary vein they enter the general circulation via the left side of the heart. Other malignant fragments in the lung may enter the bronchial vein, pass to the innominate vein and through the superior vena cava to the right heart. Here they are transported back to the lungs by the pulmonary artery.

The general circulation may also be involved through the lymphatics. The preaortic node efferents pass to the intestinal lymphatic trunk to the cisterna chyli, up the thoracic duct, to the left subclavian vein (Fig. 1).

It has been with no little interest that we reviewed 600 cases of carcinoma of the distal colon and rectum and tabulated the metastases as we found them. These were obtained by clinical methods, x-ray examinations, surgical findings, and the result of autopsy. The cases reviewed were unselected. Many of the patients had more than one admission to the hospital, giving us the opportunity to study their cases on several occasions. Our results for the most part were not the findings on one particular admission, but the findings up to when the patient was last seen in the office or hospital, or when he came to the autopsy table. Three hundred fifty-three patients were men and 247 were women. From Table I one may obtain our incidence of visceral metastases in carcinoma of the distal colon and rectum.

TABLE I. INCIDENCE OF VISCERAL METASTASES IN SIX HUNDRED CASES OF CARCINOMA OF DISTAL COLON AND RECTUM

SITE	NUMBER	PER CENT
Lymph nodes	315	52.4
Liver	155	25.8
Vagina	26	10.5
Bone	36	6.0
Bladder	34	5.6
Lungs	30	5.0
Serosal implants	21	3.5
Uterus	8	3.2
Prostate	11	3.1
Seminal vesicles	9	2.5
Brain	8	1.3
Urethra	8	1.3
Broad ligament	3	1.2
Omentum	7	1.1
Ovary	2	0.8
Heart	3	0.5
Ureter	4	0.6
Skin	2	0.3
Pancreas	1	0.1
Adrenals	1	0.1
Spinal cord	1	0.1
Aorta	1	0.1
Diaphragm	1	0.1

Lymphatic Metastasis.—Grinnell[41] states that by the time the patient is operated upon, 53 per cent of rectal tumors have metastasized to regional nodes. A high incidence of nodal spread was also found by Coller, Kay, and MacIntyre.[21] Gilchrist and David[36] quoted 62.5 per cent with nodal involvement at the time of surgery excluding those patients who had palliative surgery. Gabriel, Dukes, and Bussey[32] found 62 per cent of patients with lymph gland involvement. McVay[47] stated that 47 per cent had regional node metastases. Our incidence of nodal involvement was 52.4 per cent. Although a modified Spalteholtz technique was not used, it recently has been adopted by our department. Nevertheless the pathologist examined these specimens very closely. It is interesting to note at this point that it is not always the large node that has tumor involvement. Tumor cells have been found in the smaller nodes where inflammatory cells are the main constitutent of the larger lymph glands.

It was the opinion of Ewing[29] that all visceral metastases could be explained on the basis of tumor cells in the circulation coming to rest in any particular organ and beginning to germinate at that site. This opinion was somewhat modified by Willis,[59] who pointed out a peculiar selective distribution of metastatic tumors of certain kinds. It is not fully known if it be metabolic, chemical, or enzymic factors that determine whether or not arrested tumor particles shall germinate to produce metastases. Some tumor emboli arrested in the lung fail to grow there, but remain infertile in the occluded arterioles and undergo degeneration and fibrous organization. It is a rare occurrence, on the other hand, to find abortive tumor emboli in the liver. Skeletal muscle is clearly an unfavorable soil for germination of disseminated tumors in spite of the tremendous blood supply it receives.

Liver.—The liver usually becomes involved with secondary malignant deposits by tumor invasion of the portal vein system. Willis[60] states that in 50 per cent of necropsies on patients with all malignant tumors in the portal area, hepatic metastases are present. Although usually on the liver surface, metastatic nodules may also be found deep in the substance of the liver. Goligher[39] found that of 31 patients who had died a few days after rectal extirpation and whose livers had been thought clear of metastases at operation, 5 patients were found at autopsy to have deposits deep in the liver substance.

Invasion of the portal vein tributaries leads to further dissemination in the liver itself. We found the liver involved in 25.8 per cent of cases.

Lungs.—Willis[60] stated that the lungs are involved in one-fifth of fatal cases of carcinoma of the rectum. Brown and Warren[16] found pulmonary involvement in 38 of 170 autopsied patients. Bacon[5] cited 67 of 366 patients with carcinoma of the distal colon and rectum. Thirty-eight per cent of Abrams'[1] patients had lung metastases. On the other hand, Buirge[18] found 11.1 per cent with pulmonary involvement from carcinoma of the large intestine. In our series of 600 patients, there was an incidence of 5 per cent (30 patients) with lung metastases.

The lungs usually become involved with tumor by invasion of the hepatic veins with malignant cells and by subsequent discharging of tumor emboli to the right heart and thence to the lungs. Although usually multiple in distribution, there occasionally may be a single nodule. It is at this particular lesion that the operation of lobectomy is principally directed in palliation for pulmonary metastases.

Brain.—Next to the lung, Baker[8] found the gastrointestinal tract the most common site of the primary carcinoma in 100 cases of metastatic brain tumor studied at autopsy. The sigmoid and rectum contained the original tumor in 10 cases. Baker[7] found the large bowel to be the primary site in 8 of 114 cases.

According to Krasting,[46] the brain favors the localization of metastases, this author finding it in 5.6 per cent of 935 cases from all sites. Rau[49] recorded 3.2 per cent involvement in 851 autopsied cases of cancer. Cushing[23] stated

TABLE II. PRIMARY SITES OF ORIGIN OF CANCER IN ONE HUNDRED FOURTEEN CASES OF BRAIN METASTASES*

LOCATION	PRIMARY NEOPLASMS	LOCATION	PRIMARY NEOPLASMS
Lung	24	Eye	2
Breast	24	Liver	1
Skin	9	Thyroid	1
Kidney	9	Bone	1
Adrenal	6	Antrum	1
Colon	6	Prostate	1
Stomach	4	Gum	1
Pancreas	4	Esophagus	1
Testis	3	Turbinate	1
Uterus	5	Tonsil	1
Urinary bladder	2	Ovary	1
Rectum	2	Undetermined	4

*From Baker, A. B., and others: Metastatic Tumors of the Brain, S. Clin. North America 31: 1143, 1951.

that only about 3.2 per cent of all intracranial tumors are metastatic. Elkington[28] recorded 9 per cent, although he felt this figure was too low and should have been in the neighborhood of 20 per cent. Baker[7] quoted 17.9 per cent of intracranial tumors as being metastatic. These figures vary markedly, as some metastatic lesions are diagnosed on clinical grounds alone. Other lesions are silent and therefore unnoticed, and many skulls are not routinely opened. There will also be a variance due to the source of material studied, as a general surgical service will produce a higher percentage of metastatic brain lesions than will a neurological institution.

One of us (H. E. B.[5]), in 1940, reported 2 cases of brain metastases out of 366 cases. In our recent series there were 8 cases (1.8 per cent).

The hematogenous route is the most likely manner of spread. Rich[50] stated that the metastases occurred predominantly within the gray substance or subcortical white matter where blood supply is most abundant. From the venous circulation the tumor emboli, in order to reach the brain, must pass through the lungs. The smaller ones may occasionally pass directly through the wide pulmonary capillaries to the left side of the heart without stopping. Larger emboli suffer arrest within the lungs and may start growing to produce gross pulmonary lesions. These later may break through into the pulmonary vein and left side of the heart to produce brain metastases. Here, again, these cells may remain static. Others survive and multiply to produce lesions.

The metastases are usually scattered diffusely throughout the brain and show little tendency to localize within any particular region. Globus and Meltzer[37] found the tumor to be single in 38.6 per cent of 57 cases, multiple in 52.6 per cent, and diffuse in 8.8 per cent of cases. Just why tumor cells take hold in the cortex in one case, and in the white matter in another, is unknown. Baker's[7] distribution in 114 cases is revealed in Table III.

Our distribution in 8 cases was as follows: right cerebral hemisphere; left parietal and subcortical hemisphere; left cerebrum and cerebellum; right cerebrum; left cerebrum and cerebellum; left cerebrum; right cerebrum; the last unspecified.

TABLE III. DISTRIBUTION OF CEREBRAL METASTASES IN ONE HUNDRED FOURTEEN CASES*

LOCATION	FREQUENCY OF INVOLVEMENT	LOCATION	FREQUENCY OF INVOLVEMENT
Parietal lobe	38	Pons and medulla	10
Meninges	31	Basal ganglions	8
Cerebellum	27	Spinal cord	5
Frontal lobe	20	Lateral ventricle	4
Occipital lobe	20	Midbrain	3
Unspecified	13	Third ventricle	3
Temporal lobe	10	Optic nerve	2

*From Baker, A. B: Metastatic Tumors of the Nervous System, Arch. Path. 34: 495, 1942.

In most cases there is a remarkable resemblance between the cellular structure of the primary colon lesion and the brain metastasis. The diagnosis may be probable if the patient has a known carcinoma. Incorrect diagnoses may be: psychoneurosis, primary brain tumor, cerebral hemorrhage or thrombosis, encephalitis, or brain abscess. Cerebral symptoms of a primary tumor of the brain are usually of much longer duration prior to hospitalization than are symptoms in metastatic tumors. However, the patient is usually chronically ill, pallid, and cachectic in the majority of cases, thus providing evidence for the presence of underlying malignant disease. The brain metastasis is usually but an expression of generalized metastases.

Skeletal Metastases.—Bone metastasis from carcinoma of the distal colon and rectum is not an uncommon finding. Although not as frequent as in carcinoma of the prostate, breast, thyroid, lung, or kidney, its incidence is such that one should be constantly aware that it may occur either early or late in the course of the disease. In 1870, Curling[22] reported the first case of bony metastasis—that to the radius. In subsequent years, Hildebrande,[43] Fuzinami,[30] Goetsch,[38] and Nisnjewitsch[48] reported series of cases. Aufses,[3] in 1930, added 8 cases to the 16 already reported in the literature.

Brown and Warren,[16] in 1938, cited an incidence of 5 per cent of bony metastases in their cases. They felt that local extension played a minor role in skeletal involvement by carcinoma of the distal bowel. Further reports were forthcoming from Ghormley and Valls,[33] Bacon,[5] and Hubeny.[44] Although the latter author reported an incidence of only 0.62 per cent, he ventured the opinion that skeletal metastases may occur more frequently, as all

TABLE IV. DISTRIBUTION OF SKELETAL METASTASES IN SIX HUNDRED CASES OF CARCINOMA OF THE DISTAL COLON AND RECTUM

BONE INVOLVED	NUMBER	PERCENTAGE OF SKELETAL METASTASES	PERCENTAGE OF 600 CASES
Sacrum	14	38.8	2.3
Lumbar	13	36.1	2.1
Pelvic	8	22.2	1.3
Dorsal	6	16.6	1.0
Skull	4	11.1	0.66
Ribs	3	8.3	0.5
Sternum	1	2.7	0.16
Clavicle	1	2.7	0.16
Femur	1	2.7	0.16

patients are not subjected to a complete roentgenographic survey, nor is there always pathologic confirmation. In a recent report, Bacon and Jackson[6] reported 36 additional cases.

Bony lesions are mostly osteolytic in type, although occasionally one of the osteoblastic type is noted.

Von Recklinghausen[56] believed that embolic blocking of a vascular channel in the bone by a large mass of malignant cells was not the cause of metastases. He suggested, rather, that it was brought about by periaxial stagnation as the neoplastic cells pass from blood vessels outside the bony structure into the vascular bed within. Owing to this manner of formation, bony metastasis should occur most frequently in those subject to the greatest stress and strain as well as to temperature change.

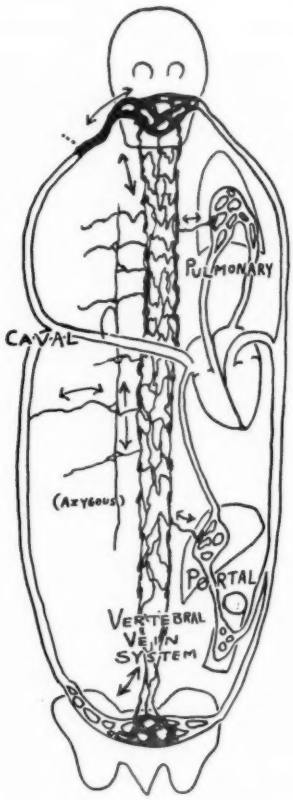

Fig. 2.—Diagram indicating the possibility of spread of tumors and abscesses from and to various regions of the body through the vertebral vein system which by-passes the caval, the portal, and the pulmonary vein system. (From Batson, O.: Function of Vertebral Veins and Their Role in the Spread of Metastases, Ann. Surg. **112**: 138, 1940.)

In 1940, Batson[9, 10] clarified many of the paradoxes of metastatic spread to the skeletal system. From his studies on the cadaver and monkey, he considered the veins of the vertebral column, cranium, and body wall a separate vein system, providing a by-pass around the portal, caval, and pulmonary vein system, yet freely communicating with them.

Batson described the vertebral vein system as a blood reservoir where these valveless veins carry blood under low pressures. During coughing, straining, or any increased activity, blood is not only prevented from entering the thorax and abdomen, but actually is squeezed out into the vertebral vein system. There is also a communication between the latter and the venal vasorum of the large vessels.

Other Sites.—Spread from carcinoma of the distal colon and rectum has been seen in other distant sites in a relatively smaller percentage of cases. Although it occurs less often in these particular locations we must remember that we are dealing with a disease that produces metastases in a manner which often seems paradoxical. This fact, however, should not deter us in removing the primary and often the metastatic lesion whenever possible in order to prolong life and to alleviate symptoms.

SUMMARY

1. Hidden metastases from carcinoma of the distal colon and rectum become more prevalent as the criteria for operability are broadened.

2. Visceral metastases from 600 cases have been presented.

3. Our efforts should not be deterred in removing every cancer whenever technically possible unless its advanced spread at the time of surgery dictates otherwise in our judgment.

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SURVEY OF INTESTINAL OBSTRUCTION

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THIS survey of intestinal obstruction is to our knowledge the first of its kind ever made in that the actual case records were submitted by thirty-five surgeons from different towns and cities. These surgeons, all members of the Central New York Surgical Society, live and work in towns and cities varying in population from 5,000 to 350,000. All of the records were analyzed by one individual. Therefore, the summary and analysis of the data, and the conclusions drawn from these records denote the opinion of one man and do not necessarily represent the opinions of the group as a whole.

Four hundred thirty-nine individual case records were reviewed, 278 cases of small bowel obstruction, 161 of large bowel obstruction. These two classes were reviewed separately.

Inquiry was made into the etiology of the obstruction, duration of obstruction prior to hospitalization, and operation; the mechanism of obstruction, the level of obstruction, the type of intubation, success and duration of suction when used; the findings at operation and the operative treatment carried out; the type and amount of antibiotics used, the seriousness of electrolyte problems, and the complications and mortality encountered.

The commonest cause of obstruction in this series, as in other recently reported series, is postoperative adhesions, closely followed by external hernias. There was quite a large group of adult patients (42) who developed obstruction without external hernia and without previous surgery. Intussusception and congenital anomalies made up a small group. Surprisingly, the mortality rate for each of the three more common groupings, external hernia, postoperative adhesions, and "no previous operation," is almost identical from 5 per cent to 8 per cent. That congenital atresia is a serious disorder is attested by the fact that there was but 1 survivor among 4 such patients.

Gangrene of the bowel is the most important factor predisposing to morbidity and mortality. There were 12 deaths among 45 patients whose bowel had become gangrenous. If we exclude from consideration the cases of atresia, the hopeless cases of cancer, and the gangrenous cases, the over-all mortality is less than 3 per cent. In fact, in the groups of cases comprising late postoperative adhesive obstruction, external hernias, and "no previous operation," there were but 3 deaths among 168 patients whose bowel was viable.

When considering the level of obstruction in the three most common groups, we find 94 per cent of cases (in which the level of obstruction was stated) involved obstruction in the terminal ileum. In the more restricted group of

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postoperative adhesions, 90 per cent involved the ileum. The paucity of cases of high obstruction undoubtedly accounts for the fact that severe electrolyte imbalance was an infrequent occurrence.

Among the patients succumbing after operation for intestinal obstruction, one-third of the mortality is owing to peritonitis, usually secondary to gangrenous bowel.

Although phlebitis and embolism were not unusual, only 1 death could be attributed to embolism and that in a hopeless case of carcinoma. There were 2 patients who developed coronary thrombosis, 2 cerebral thrombosis, and 3 who died of peripheral vasomotor collapse, which might well have been "toxemia shock." Severe pulmonary complications were unusual, 4 per cent, although 1 patient died of aspiration of gastric content. Severe wound infection was remarkably infrequent—less than 5 per cent. There were but 2 cases of wound dehiscence in the entire group of patients with small bowel obstruction. Severe electrolyte imbalance was either not encountered, or at least was corrected well enough so that it could only once be suspected as a cause of death. It is possible, however, that the mortalities attributed to "toxemic shock" may have been due in part to some electrolyte disturbance.

The low incidence of wound complications, 5 per cent, and the relatively few intraperitoneal abscesses reported probably are due to the liberal use of antibiotics. Although a statistical study is not possible, penicillin or a combination of penicillin and streptomycin was used in the case of almost every patient showing gangrene. Less commonly, Aureomycin, Chloromycetin, and terramycin were employed. The fact that there still was a mortality rate of 27 per cent in patients exhibiting gangrene shows that the presently used antibiotics are not the complete answer. Apparently there is something elaborated from the interaction of bacteria and dead bowel which at least is poorly controlled by our present antibiotics. It is significant that 7 of the 12 deaths in patients exhibiting gangrene occurred within 48 hours.

INGUINAL HERNIA

The first golden 24 hours is no protection against gangrene of the bowel in external hernia. In this series 6 of 19 patients past the age of 50 years exhibited nonviability of the bowel which had been strangulated less than 24 hours. In fact, a bowel which had been strangulated for only 3 hours in one case was nonviable. In general, however, the longer the obstruction the greater the chance of gangrene. It simply implies that when one is dealing with strangulated hernia, hours, not days, are the prime consideration. That one cannot determine the state of the bowel which may be reduced is emphasized by the case of a patient in whom an inguinal hernia was reduced nonsurgically. Two weeks later the abdomen was explored, a Richter's hernia found, and necrotic bowel resected, fortunately, with a good recovery.

FEMORAL HERNIA

Of all the causes of small bowel obstruction, femoral hernia is the most serious. One-half of the patients, 12 out of 25, showed gangrene; 3 died. These

hernias are notoriously difficult of diagnosis. In fact, in 6 out of 25 patients the diagnosis was missed for at least 24 hours. In 5 of these 6 patients the bowel was gangrenous; 2 died. In 3 patients there was no external hernia, in the other 3 it was so small and insignificant not to be immediately appreciated. There were 4 hernias of the Richter's type in this group of femoral hernias.

VENTRAL HERNIA

There were 12 ventral hernias, 2 umbilical hernias with a total of 6 complications and 1 death. In this group the most serious hernia appeared to be that about a previous colostomy. Two of these entailed resection, 1 of almost the entire small intestine. The 1 death was in an elderly obese woman who had an "acutely incarcerated huge ventral hernia" of 3 days' duration. An unsuccessful attempt was made for 48 hours to relieve obstruction by suction (the tube never passed the stomach). The patient died 48 hours postoperatively.

"NO PREVIOUS OPERATION"

Wangensteen has called attention to the seriousness of intestinal obstruction in the absence of a scar on the abdomen. In this series gangrene was slightly less common, 3 in 42, than in those with a previous scar, 17 out of 78. However, it can be stated that in only 4 cases could suction be effective in relief of the obstruction. Even without external scar or hernia, bands or adhesions still account for the majority of obstructions (25 of 42 in this group).

INTUSSUSCEPTION

There were 12 cases of intussusception. The age of these patients ranged from 2.5 weeks to 45 years. Seven of them were under 1 year. Nine were ileocecal, 3 were ileoileal. One patient, aged 11 years, with ileoileal intussusception, required resection because of gangrene. Meckel's diverticulum was responsible for intussusception in 2 cases. Although there was no mortality, 1 patient suffered a recurrent intussusception 3 months after the original operation, and 1 patient developed an adhesive obstruction 6 months after the intussusception.

INTUBATION AND SUCTION

The use of intestinal suction in the definitive treatment of intestinal obstruction is the subject of much controversy. In fairness, we are sure that many patients with suspected early obstructions were promptly relieved by intubation and suction and, since the diagnosis was not proved, they were not included in this series. A variety of tubes was used, Wangensteen, Miller-Abbott, and Cantor being most popular. Some men had active fluoroscopic acid, others did not. Among 147 cases in which suction could have been used as definitive therapy, it was sustained for at least 24 hours in 57 cases—with relief of the obstruction in 17 or practically one-third of the patients. There were 4 patients so treated whose bowel proved to be gangrenous. Each of these 4 patients survived after resection of the affected bowel.

AGE AND MORTALITY

An over-all mortality rate of 8 per cent (23 patients) attests to the serious nature of obstruction of the small bowel. In addition, practically one-fourth of the patients (23 per cent of 62 patients) developed a complication of note. That age is a real factor in mortality is proved by the fact that (if we exclude congenital atresia) there were but 3 deaths among 121 patients under the age of 50 years, whereas there were 17 deaths among 153 patients over the age of 50 years.

OBSTRUCTION OF THE COLON

As in all other reported series, carcinoma is the leading cause of obstruction to the colon, approximately two-thirds of the obstruction owing to this cause, although in only 53 of the cases the obstruction was classified as complete. All 110 patients suffering carcinoma underwent emergency operation for obstruction without benefit of preparation with enteric antibiotics. Diverticulitis was a fairly common cause of obstructions, although few of these obstructions were complete. Volvulus, although somewhat rare, was very serious in its behavior. It is noteworthy that one-fourth of all patients suffering obstruction to the colon developed a serious postoperative complication, and one-eighth of the patients died. Age per se was not a great factor in morbidity or mortality.

The one lethal factor in obstruction of the colon seemed to be imminent or actual perforation of the cecum. For many years it has been standard therapy to perform some decompressive procedure prior to removal of a carcinoma which completely obstructed the colon. Cecostomy was carried out in 21 patients of this series with 5 deaths, colostomy in 14 patients with 1 death. In 4 of the patients treated by cecostomy, the cecum had perforated prior to operation. Three of these patients succumbed. A fourth patient in this group had been obstructed for 10 days prior to operation and the cecum was very thin and obviously devoid of blood supply. This patient died. The 1 death in the group of 14 treated by colostomy was in the patient whose bowel had been obstructed for 2 weeks. At operation there was a gross perforation of the sigmoid colon.

Thus although there were 6 deaths among 35 patients treated by conservative surgical decompression, 5 of the deaths occurred in patients whose bowel was gangrenous or perforated at the time of operation.

There were 12 patients upon whom resection and anastomosis was performed in the face of complete obstruction. There were 2 deaths, 1 in a patient with a carcinoma of the sigmoid, whose obstruction was of 4 days' duration. This patient succumbed of a pulmonary embolus. The other patient had a carcinoma of the right colon; the obstruction was of only 8 hours' duration, yet a perforation of the cecum had occurred with peritonitis at the time of surgery. This patient succumbed of shock.

There were 5 patients whose obstructing carcinoma was simply exteriorized. All of these patients survived. There was 1 colocolostomy performed for a nonresectable carcinoma. This patient survived. Although there were 8 deaths

among 53 patients with acute obstruction of the colon, it was found that there were only 2 deaths among 46 patients who had not developed perforation or gangrene of the bowel prior to operation. That perforation of the colon prior to surgery portends a grave prognosis is attested by the fact that there was but 1 survivor out of 7 in this group.

In the group showing only partial obstruction and submitted to resection and anastomosis, a mortality of 5 among 17 patients seems unduly high. There were 2 patients whose deaths could be attributed to a leakage of the anastomosis (1 from a duodenal leak in a really inoperable case), 1 attributed to a poor renal reserve (well appreciated by the surgeon prior to operation), and 1 following pulmonary embolism. Exteriorization procedures were carried out in 9 cases with only 1 serious complication.

Sepsis, peritonitis, and shock—all a consequence of perforated or gangrenous bowel—were responsible for two-fifths of the complications and one-half of the deaths following operation for obstruction of the colon. Pneumonia was uncommon, 2 per cent. Thrombosis and embolism account for one-fourth of the complications and 3 of the deaths. Considering the age group with which we were dealing, cardiac and renal failure were surprisingly infrequent. There were but 2 cases of dehiscence, neither fatal.

COMMENTS

The over-all mortality rate of 8 per cent in small bowel obstruction and 12 per cent in colon obstruction compares very favorably with other published reports. The chief improvement in mortality in this series over those published prior to 1945, however, appears in nongangrenous obstruction. In fact, whenever the bowel was viable there was no difference in the mortality rate whether the obstruction was strangulatory or not.

The mortality rate of 3 per cent in nongangrenous obstruction compares very favorably with that occurring in other types of abdominal surgery. In cases with obstruction of the colon it appears that the risk of operation is quite minimal, less than 5 per cent, if the obstruction has not progressed to the point of perforation.

Most of the mortalities in this group can be charged to: (1) failure to recognize strangulatory obstruction until it had progressed to gangrene, (2) delay in operative treatment for obstruction of the colon until the bowel had progressed to imminent and in many cases actual perforation.

In spite of the many well-known signs and symptoms of strangulatory obstruction, strangulation and gangrene often occur without the classical findings. It would appear that a prolonged attempt to relieve obstruction by intubation is not justified, except in the early postoperative period. Since strangulation in external hernias may occur in a very few hours, immediate operation should be advised in every acutely incarcerated hernia. Because femoral hernias are so easily missed, special care should always be taken in every case of bowel obstruction to search for such a hernia. Attention is called to the fact that in one-fourth of those cases such a hernia was missed for over 24 hours.

The time-honored methods of surgical decompression of the colon, cecostomy and colostomy, were usually used in the treatment of obstruction of the colon, and in those cases in which perforation had not occurred, the morbidity and mortality rates were remarkably low. Attention is called to the group, 17 in number, in which resection was carried out, with or without anastomosis, in the face of complete obstruction. Prior to the availability of antibiotics such an attack had been well proved to be unduly hazardous. In this group there were 2 instances of perforation prior to surgery. There were 2 deaths, 1 in a patient with prior perforation, the other occurring from pulmonary embolism. The relatively high mortality rate following resection in cases of partial obstruction, it seems, points out that the state of the bowel is the important thing to consider. At the time of operation, if the tone of the bowel is good and its viability is unimpaired, it is my personal opinion that resection and anastomosis can be safely carried out even in the face of acute obstruction. This is particularly true of obstruction of the right and transverse portions of the colon, in which cases the entire obstructed segment can be removed, as suggested by Baronofsky. Contrariwise, even if obstruction is not complete, if the bowel has lost its tone and is edematous, surgical decompression may be necessary before resection of the lesion becomes safe.

In a review of this type it is obvious that intestinal obstruction was managed in many different ways. In general there was a tendency for early operation in the smaller communities and a greater emphasis on the preparation of the patients in the larger cities. In fairness to both plans of therapy it must be said that there were patients submitted to prompt surgery on admission who died of fulminating peritonitis and shock; there were also patients in the second group who were temporarily relieved by suction whose obstruction recurred, and who died following operation for a recurrent obstruction. In general, early surgery after a few hours spent in correction of the patient's disturbed physiology seems to be the best plan of attack.

TABLE I. INTESTINAL OBSTRUCTION

	NUMBER	NUMBER OF MORTALITIES
	Small Intestine	
External hernia	93	7
Postoperative adhesion	110	9
No previous operation	42	2
Intussusception	12	0
Atresia	4	3
Other	17	2
	278	23 (8 per cent)
	Large Intestine	
Carcinoma	110	16
Diverticulitis	16	0
Bands and adhesions	10	0
Hernias	5	0
Miscellaneous	20	4
	161	20 (12 per cent)
Total	439	43 (10 per cent)

SUMMARY

Four hundred and thirty-nine cases of intestinal obstruction in upstate New York occurring in the two-year period ending July 1, 1951, have been reviewed.

Small Bowel Obstruction.—There were 278 cases of small bowel obstruction with 23 deaths for an over-all mortality rate of 8 per cent.

Among 168 adults admitted to the hospital for intestinal obstruction due to adhesions, external hernia, and "no previous operation," if the bowel was viable at time of operation, there were but 3 deaths.

There were 12 deaths among 45 patients exhibiting gangrene of the bowel.

Over 90 per cent of obstructions were found in the terminal ileum.

At the time of surgery 25 of 93 external hernias exhibited gangrene of the bowel. The mortality in cases of external hernias and obstruction due to late postoperative adhesions was practically the same, 7 of 93 and 6 of 78, respectively.

Obstruction of the Colon.—There were 20 deaths among 161 patients with colonic obstruction. Carcinoma was the usual cause of obstruction of the colon, occurring in 110 of the total 161 cases. Obstruction was complete in 53 cases of cancer, incomplete in 57 cases of cancer. Operation was carried out in 46 patients with complete nonperforating obstruction of the colon, with 2 deaths. In 7 cases the bowel had perforated or was gangrenous; 6 patients died.

Resection of the bowel was carried out in the face of complete obstruction (usually early) in 17 patients with 2 deaths; 2 of these showed perforation at the time of operation; 1 died. Decompression was carried out by cecostomy or colostomy in 35 patients with 6 deaths, and in 29 patients without gangrene or perforation with 1 death.

CONCLUSIONS

1. Gangrene or perforation of the bowel is the most important lethal factor in intestinal obstruction today.

2. The mortality from nongangrenous obstruction is minimal.

3. Earlier diagnosis of strangulatory obstruction and of complete colonic obstruction is the key to decreasing mortality in intestinal obstruction.

The writer wishes to express his genuine appreciation to the many surgeons of the Central New York Surgical Society whose cooperation made this survey possible.

DUODENAL INTUBATION

JOHN W. DEVINE, M.D., AND JOHN W. DEVINE, JR., M.D., LYNCHBURG, VA.

THE mechanics of intubation of the duodenum is a major, unanswered question in dealing with intestinal obstruction. This is the only assignment in modern surgery that the professor delegates to the resident, and he, in turn, passes it down to the intern. If the professor were asked by the intern to demonstrate this assignment, he would be embarrassed. Our interest in solving this problem has been increased because of the difficulty and sometimes failure of intubation in the most needed case along with the danger of exposure to scattered radiation by the patient, radiologist, and surgeon. One should read the exhaustive studies of Cilley, Leddy, and Kirklin[1-4] concerning the protection problem under the fluoroscope. The most important conclusion derived from their studies is that exposure of the radiologist can be held to a minimum by using the smallest field of the radiation commensurate with any particular task. It goes without saying, that the examination should be carried out as expeditiously as possible. This was impossible in the past with our methods of intubating the duodenum.

In reading an article in one of the popular lay magazines on the headaches of a government official, whose duty it was to rule on request for a priority material, "Alnico Five," used as a fixed magnet in radar, television, radio, and other fields, our interest was aroused in using this magnet as an aid in intubating the duodenum. One example of the strength of this magnet, which was very impressive, was the account of how a magnet, only five inches high, was able to bring an outboard motor to the surface of three hundred feet of water. This revelation broke the mental yoke that magnets could not work in guiding a tube through the stomach to the duodenum. This yoke originated from the discarded electromagnet used forty years ago in Kirschner's Clinic in Tübingen, which had failed. This magnet was reported to be as large as a piano.

We had previously tried electromagnets without success. This knowledge of the modern, powerful fixed magnets encouraged us to renew our experiments along this line.

With the cooperation of Mr. M. E. Strieby of the American Telephone and Telegraph Company, and Mr. Charles Maynard of the Indiana Steel Corporation, we have found that a magnetic tip, made of high magnetic, permeable metal, when used with an Alnico Five* fixed magnet, would, in some individuals, attract the tip of the tube to the magnet through the abdominal wall. This gives complete control of the position of the tube in the stomach. This observation is prematurely reported in order to encourage other investigators with more clinical material and resources to join us in this investigation.

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*Manufactured by the Indiana Steel Corporation, Valparaiso, Ind.

The magnets used have been extremely sensitive and must be handled with great care. One must apply the protectors immediately following each use and be careful not to drop the magnet, as this could weaken it. To allow the unprotected magnet to lie on its side against metal is one of the greatest abuses to which the magnet can be subjected. We are encouraged with our limited experience with this magnetic tip and Alnico Five magnet, and feel that it will eventually be the solution to this difficult problem.

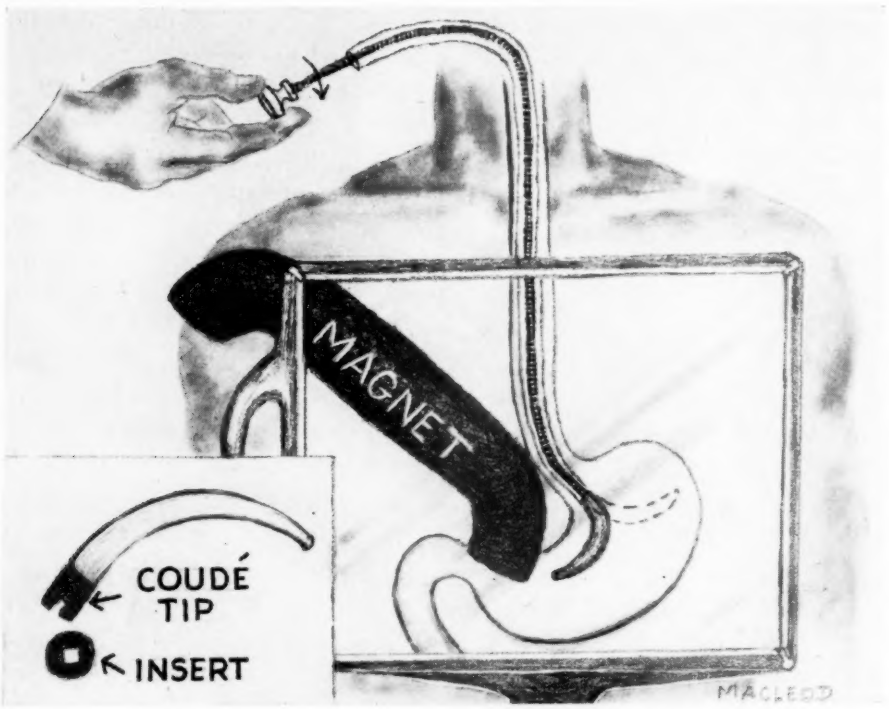

Fig. 1.

Another project along the same line that is being studied in our laboratory is the use of magnetic capsules, which consist of metal rods the size of a No. 5 capsule, with a small hole through the center. This hole is threaded by a special Nylon thread, and the rod placed in an empty capsule. The patient swallows the capsule and, with the aid of the Alnico magnet, the capsule is manipulated through the duodenum under fluoroscopic visualization. Then a small plastic tube is inserted in the nose and the silk is brought back out through the nose. The silk is threaded through an air vent tube,[5-7] and the tube is inserted into the nose. A magnetic metal tip is used on the air vent tube, and, with the help of the magnet, the tube is guided to the region of the pylorus. The magnet is then used to fix the capsule, which is in the duodenum or the jejunum, so that it will not pull out when the tube is guided through the pylorus. The string acts as a filiform guide. This latter maneuver is performed under the fluoroscope and is completed in a relatively short period of time. This method also has great possibilities but needs further trial.

The Grafton Smith stylet,[8] a most ingenious instrument, has been used on several occasions. We have been a little heavy handed with this delicate instrument, which has resulted in several broken control wires. However, this ingenious instrument should be included in the armamentarium of every surgeon who is faced with the most difficult problem.

Positioning the patient is always used, but it is our opinion that we are lucky rather than skillful even when this works. So often it is in the patient for whom we so desperately need to intubate the duodenum that this method fails so miserably.

By placing a rubber catheter with a fixed curve (Coudé Tip) on the tube and using a flexible cable[9] to turn and advance this tip, we have been able to intubate the duodenum when all other methods have failed.

CONCLUSION

The various known methods used to intubate the duodenum have been reviewed. The problem is not yet definitely solved, but the use of magnetic tip tubes and magnetic tip capsules controlled by the Alnico Five magnet have been most encouraging.

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THE "OBSTRUCTED" MILLER-ABBOTT TUBE

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THERE are few things more disheartening in the treatment of intestinal obstruction than to have successfully passed a Miller-Abbott tube into the small intestine and to have it fail to aspirate the intestinal contents. Fortunately, this problem rarely presents itself. The source of the difficulty appears to lie in the consistency of the intestinal contents, for the ease of instillation of water or other solutions has repeatedly proved the patency of the lumen of the tube. After much trial and error, a simple solution to the problem presented itself. This consisted in the instillation of a proteolytic ferment (Caroid) through the tube into the small bowel. Three cases are reported to illustrate the effectiveness of a Caroid solution in overcoming the quandary resulting from a nondraining double lumen tube.

CASE REPORTS

CASE 1.—K. W., a 59-year-old white man, was admitted complaining of abdominal cramps of one month's duration. At the onset of his illness the attacks occurred at two- to three-day intervals. There was a gradual increase in the frequency of pain and, on admission, the attacks of crampy abdominal pain recurred every five to thirty minutes. The patient's physician had placed him on a strict milk diet which he had maintained faithfully for three weeks prior to admission. A scout film of the abdomen revealed a stepladder pattern of the small bowel and very little evidence of gas in the large bowel.

A Miller-Abbott tube was passed into the jejunum shortly after admission. There was no drainage from the tube during the night, although the tube was irrigated frequently with a saline solution. The tube was removed eight hours after its insertion and a second Miller-Abbott tube was passed into the small bowel. Although frequently irrigated, only 200 c.c. of fluid drained from the tube during the next forty-eight hours. Twenty-five cubic centimeters of a 10 per cent solution of Caroid was then instilled into the Miller-Abbott tube and the tube was clamped for fifteen minutes. On release of the clamp, 300 c.c. of intestinal contents was aspirated within the next hour. Thereafter, the Caroid solution was instilled only when drainage ceased. The patient was successfully deflated in the next twenty-four hours. At operation, an annular carcinoma of the splenic flexure was found.

CASE 2.—E. H., a 63-year-old white woman, was admitted for the treatment of her third episode of intestinal obstruction due to carcinoma of the ovaries with gastrointestinal metastases. On admission a Miller-Abbott tube was passed into the jejunum, but little was aspirated for the first forty-eight hours. A 10 per cent solution of Caroid was then instilled into the tube and 2,270 c.c. of fluid was aspirated in the following twenty-four hours. The patient died twenty-four hours later, and at autopsy the obstructed small bowel contained a large amount of thick, mushy material of such a consistency as to make aspiration through a small lumen tube difficult.

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CASE 3.—P. M., a 43-year-old white man, was admitted for the treatment of his second episode of intestinal obstruction due to carcinoma of the cecum with metastases. A Miller-Abbott tube was passed into the jejunum, but it failed to aspirate any fluid. The tube was irrigated with a saline solution without success. Thirty cubic centimeters of a 10 per cent solution of Caroid was then instilled at fifteen-minute intervals and, after forty-five minutes, 200 c.c. of a bloody fluid returned. Following this, drainage was continuous until the patient was explored. At operation the small bowel was found to be adequately decompressed.

DISCUSSION

The contents of the normal small bowel are of such consistency as to pass easily through the Miller-Abbott tube. In the obstructed small bowel, this fluidity is usually maintained. However, in an occasional patient, as shown by the autopsy in Case 2, the particulate content of the obstructed small bowel is of such size as to prevent easy aspiration. In such instances a proteolytic ferment will permit the intestinal tube to function properly by digesting the large particles. Caroid, a commercial preparation of papain, obtained from the fruit of Carica papaya, is ideal for this purpose, since it acts in an acid, neutral or alkaline medium to convert proteins to amino acids.[1] A 10 per cent solution can be used in 30 to 60 c.c. amounts repeated at fifteen- to thirty-minute intervals until drainage is established. This enzymatic action of Caroid has also been successfully employed in the treatment of esophageal obstruction due to food impaction.[2]

SUMMARY

Three case reports are presented, showing that a proteolytic ferment will promote drainage through a poorly functioning intestinal tube.

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AUTOGENOUS AORTIC GRAFTS FASHIONED FROM A SMALLER ARTERY

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ALTHOUGH resection of coarctation of the aorta has become a well-established procedure following the work of Crafoord[1] and Gross,[2] there are unusual cases in which a direct end-to-end anastomosis cannot be performed after the constricted portion has been excised. When the proximal and distal ends of the aorta cannot be brought together, either the subclavian artery has been swung down to the distal aorta, or a graft has been used to bridge the defect. The first of these alternatives has not given satisfactory results in alleviating the hypertension. The second procedure has given excellent immediate results, but long-term evaluations are yet to be made.

Autogenous blood vessel grafts are preferable because they have been shown to persist as structures almost identical to normal vessels. Miller and associates,[3] in reporting on arterial grafts in small arteries, stated that "arterial autografts persist as viable segments of artery which are almost indistinguishable grossly and microscopically from the adjacent normal recipient artery." Johnson and associates[4] found aortic autografts in the pig to have the same appearance as recipient aorta above and below the graft.

Likewise, autografts to the aorta would be most desirable were it not for the fact that in the human body there is no artery the size of the aorta. We wish to offer a method of supplying an autograft of large enough diameter to be applicable to the treatment of coarctation of the aorta when only a short graft is needed. This procedure involves fashioning a graft of large diameter from a long length of a small artery by longitudinal splitting of the long-excised small artery and suturing the short sides of the rectangular piece of vessel together (Fig. 1). The diameter of the newly formed vessel is theoretically equal to the length of the small artery divided by 3.1416, but actually a slightly longer segment is necessary. The length of the newly formed segment is the diameter of the small artery times 3.1416. The main disadvantage of this method is the resultant short length of the graft. In coarctation of the aorta, the internal mammary artery is always available for fashioning one of these short, large-diameter grafts.

We present here experimental work in support of this method as well as measurements and observations on its applicability to human coarctation of the aorta.

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EXPERIMENTAL PROCEDURE

Mongrel dogs varying in weight from 15 to 20 kilograms were used. The left femoral artery was excised to make the graft, which was transplanted to the abdominal aorta below the origin of the renal arteries. The dogs were anesthetized with intravenous Nembutal. The skin of the abdomen and inner surface of the left femoral region were shaved and prepared with soap, water, 2 per cent iodine, and alcohol.

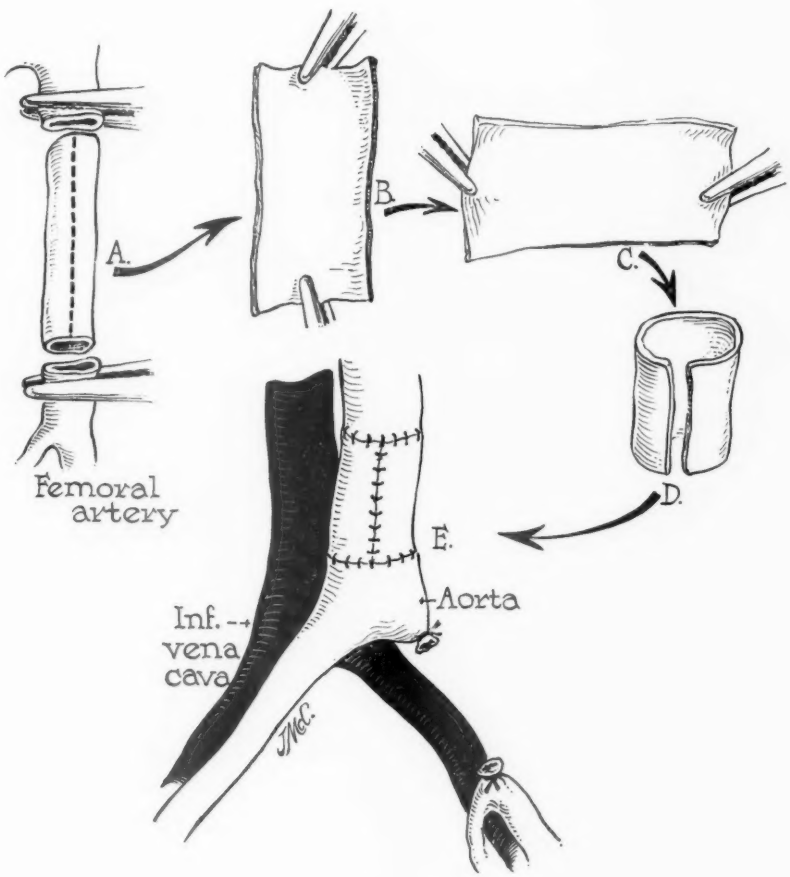

Fig. 1.—Technique of fashioning autogenous aortic grafts.

Extraperitoneal approach to the aorta from the left side largely eliminated the annoyance of having the bowels crowd into the operative field. The aorta below the renal arteries and proximal to its bifurcation was exposed and several lumbar branches isolated, doubly ligated, and divided. The diameter of the aorta was measured. A length of femoral artery 3.5 to 4 times the diameter of the aorta was isolated and all branches to this segment were ligated and divided. After proximal and distal ligation of the vessel, this segment was excised. The femoral artery was then split lengthwise making a rectangular piece of vessel. The rectangle was then fashioned into a vessel by suturing the

two short sides together with a continuous over-and-over stitch of 000000 silk. The newly fashioned vessels then had a length equal to the circumference of the original femoral artery, and a diameter approximately equal to the measured aorta.

The aorta was then doubly clamped with Potts coarctation clamps fitted into the vise holder, and a segment of aorta excised or the aorta simply transected. The newly fashioned vessel graft was sutured in place with 00000 or 000000 Deknatel silk. The graft was fixed in position by placing four sutures—one at each angle. Both anterior sides were coapted with continuous sutures. Then

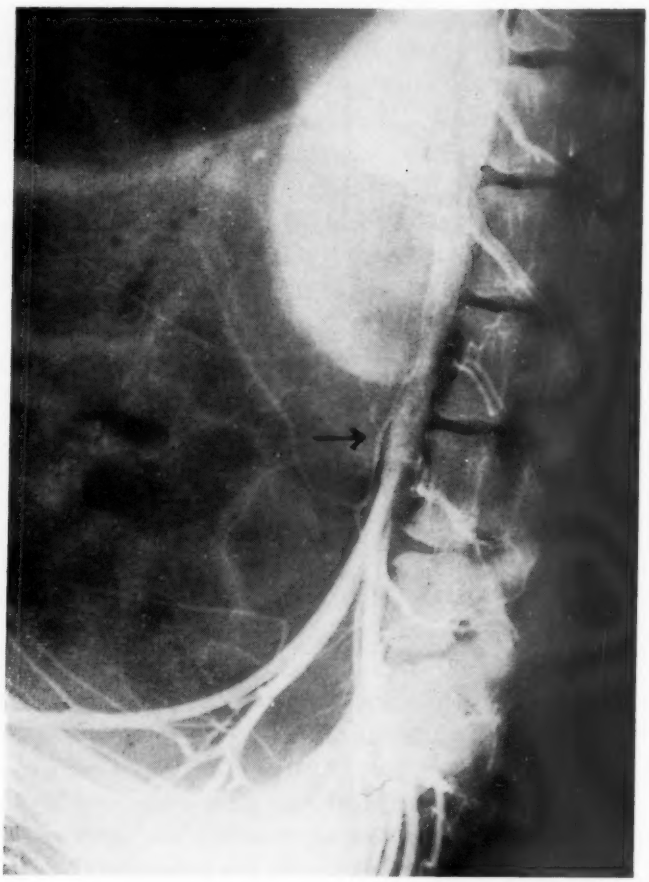

Fig. 2.—Angiogram made six weeks after operation. Arrow indicates site of graft.

the clamps were swung over and the posterior sides were sewed, each with another continuous suture. In other words, the sutures were interrupted twice in sewing each end of the graft in place. The juncture of the vertical suture line in the graft and the transverse suture line between graft and aorta did not offer any unusual difficulty. The lower clamps were released slowly, and hemostasis of small leaks in the suture line was obtained usually by slight pressure and waiting. Occasionally an additional stitch or two was thought neces-

sary for control of bleeding. Only on very few occasions did the vertical suture line of the graft itself give rise to leakage. At the conclusion of the procedure there was always brisk pulsation in the distal aorta. The wounds were closed with catgut without drainage. A good femoral pulse was always sought for and found on the right after the wounds were closed. Duracillin 300,000 units was given to most dogs the first day. No coagulants of any kind were used postoperatively.

During the postoperative periods, persistence of a normal right femoral pulse indicated an open aorta. At various lengths of time following operation four dogs were anesthetized with Nembutal and angiograms of the abdominal aorta and graft were made. Diodrast was injected through a polyethylene catheter passed down the carotid into the aorta or up the femoral artery past the graft site. Slight constriction was noted at the suture lines but a good channel was demonstrated in all (Fig. 2). After angiography was completed, the animals were sacrificed and observations were made on the fresh post-mortem specimens (Fig. 3). Blocks of tissue for microscopic study were obtained after fixation of the specimen in Zenker's solution. Blocks were embedded in paraffin, cut and stained with hematoxylin and eosin, Mallory's aniline blue, and Weigert's elastic tissue stains.

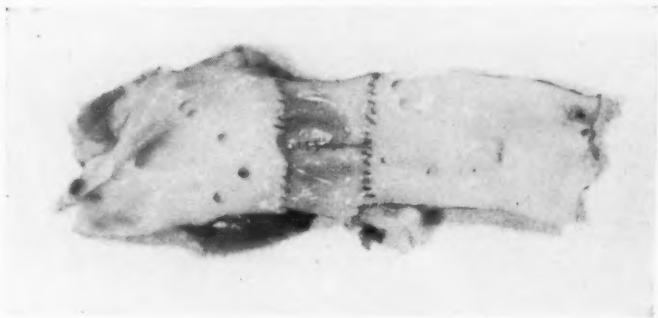

Fig. 3.—Specimen of aortic graft six weeks after operation.

RESULTS OF EXPERIMENTS

Implantation of grafts in the manner described was performed on nineteen consecutive dogs all of whom survived the operation. Six dogs living in good health are to be sacrificed at later dates to obtain long-term specimens. Nine dogs have been sacrificed at intervals from one day to sixteen weeks.

There were four frank failures. Two dogs died at five days and seven days following operation of thrombosis and hemorrhage, and two dogs died at five and twelve days of overwhelming local infection.

PATHOLOGY

Gross.—No observable changes were noted in grafts removed in the first few days after operation. There were no thrombi in the successful experiments. Lumina were of good size without constriction or dilatation. The internal

surfaces of the grafts were smooth. In the surrounding tissues there were serosanguineous exudate and evidence of local tissue reaction. In the specimens taken at three, six, and sixteen weeks no thrombi were noted on the grafts or at the suture lines. In the five- and twelve-week specimens there were a few small areas of reddish brown discoloration on the graft. However, the intima appeared smooth in all specimens. The five-week specimen showed a darkened discolored area at the mid-point of the vertical suture line in the center of which was a yellow plaquelike area. Gross observation suggested organization of a small thrombus. In dissecting the grafts and aorta from the surrounding tissues at post-mortem examination the graft was indistinguishable from the adjoining aorta and usually had to be identified by the black silk sutures. Tissue reaction was not excessive, only minimal dissection being required to free the specimens.

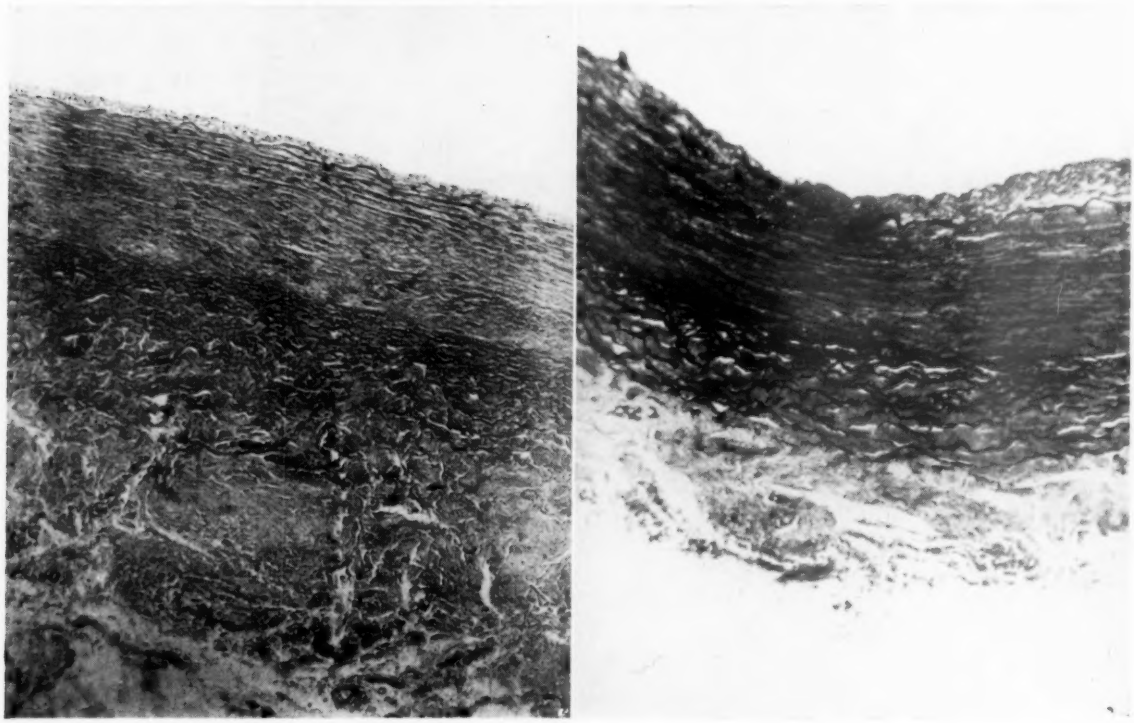

Fig. 4. Fig. 5.

Fig. 4.—Hematoxylin and eosin stain of microscopic section of autogenous graft taken sixteen weeks after operation shows unchanged intima and media.

Fig. 5.—Weigert's elastic tissue stain of autogenous graft sixteen weeks after operation shows the elastic tissue intact.

Microscopic.—The smooth muscle of the arterial wall persisted as living cells without apparent diminution in number. Up to sixteen weeks no fibrous replacement of the media was observed (Figs. 4 and 5). In only one specimen (five weeks) was there a suggestion of thinning of the muscle layers. The loss of endothelium noted in the first few days after operation was later replaced by cells which evidently grew in from the intima of the adjoining aorta. The

intimal cells were frequently observed to be several layers in depth. The internal elastic membrane was intact except where it was surgically severed.

Surrounding the outer surface of the graft in the early postoperative period was an acute inflammatory response, which later subsided. The small yellow plaque observed grossly in the five-week specimen proved on microscopic examination to be an infected thrombus.

It was concluded that the autogenous grafts maintained an adequate functional and anatomical channel of approximately the same size as the recipient aorta, and that during the short period of observation the muscle and elastic tissue of the graft persisted as living tissue and did not undergo degenerative changes or fibrous replacement.

CLINICAL APPLICATION

In considering the possible future application of such a graft to coarctation of the aorta, we made vessel measurements in two recent clinical cases neither of which required a graft.

Case 1 was that of a 15-year-old male youth.

1. Diameter of aorta proximal to left subclavian artery	21 mm.
2. Diameter of left subclavian artery	18 mm.
3. Diameter of aorta immediately proximal to coarctation	13 mm.
4. Diameter of left internal mammary artery.	6 mm.

A segment of internal mammary artery 70 mm. long was dissected free and excised. The calculated length necessary to fashion a graft 13 mm. in diameter was approximately 45 mm. It must be borne in mind that an artery will contract considerably after it is resected. When measuring the length of vessel necessary to provide a graft of suitable circumference it is well to put the vessel on a bit of stretch or the graft will bulge when it is exposed to arterial pressure. This graft would have served to bridge a gap approximately 18 mm. in length (3 by 6 mm.—the diameter of the internal mammary artery) had it been necessary.

Case 2 was that of an 8-year-old male child.

1. Diameter of aorta proximal to left subclavian artery	10 mm.
2. Diameter of left subclavian artery	10 mm.
3. Diameter of aorta immediately proximal to coarctation	10 mm.
4. Diameter of left internal mammary artery	5 mm.

A length of internal mammary artery 40 mm. long was easily available but was not removed. It would have been of sufficient length to fashion a graft the necessary 10 mm. in diameter, and would have furnished a graft 15 mm. in length.

Clinical applicability of autogenous grafts made of small diameter arteries is unknown. These preliminary animal experiments, however, suggest the possibility of their use when a short graft is needed. Long-term studies will determine whether all the elements of the graft will continue to live and be able to withstand the strain of aortic pressure.

SUMMARY

1. A method of fashioning a large autogenous graft from a small artery has been proved feasible experimentally.

2. Such grafts may be useful when a short gap needs to be bridged after resection of a coarctation of the aorta.

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SPECIFIC TRANSFUSION THERAPY

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THE routine use of whole blood for transfusion without consideration of the specific indication for its components, cells and plasma, is not rational therapy. In many instances the physiologic needs of the patient are not properly corrected. It is important not only to utilize the component of blood best suited to correct the deficiency, but also to give it in doses calculated on the basis of the patient's requirement. While 500 c.c. of whole blood is considered to be the safe amount which may be withdrawn from the donor, it does not represent the required dose of blood for the recipient. Likewise the need of a patient may be for the cellular component of whole blood, in which case the plasma contained in the transfusion will not serve a useful purpose and may actually be harmful to the patient. On the other hand, certain patients will require the plasma component only, and the cells transfused may serve no useful purpose or may cause untoward symptoms.

Since 1948, 99,200 blood transfusions have been issued from the Blood Bank of Dade County. Approximately 71 per cent of the transfusions administered have been whole blood. The remaining 29 per cent or 28,750 transfusions have been approximately one-half cell suspension and one-half plasma, resulting in a 15 per cent saving in blood (Table I).

In addition to this economic advantage, we feel that the clinical advantages of specific transfusion therapy are great. It is especially important in bad-risk patients requiring massive and multiple transfusions that the proper amount and proportion of the components, cells and plasma, be administered.

Figs. 1 to 4 illustrate indications for the transfusion of whole blood and its major components, red cells and plasma.

WHOLE BLOOD TRANSFUSIONS

The most obvious indication for the use of whole blood is, of course, for replacement of whole blood loss as in hemorrhage; the chief modification is the urgency of replacement, in which case plasma finds its greatest usefulness. In chronic blood loss the opposite is true, and replacement considerations are hemodilution, normal blood volume, and planned operative therapy.

In massive concealed hemorrhage, such as in ruptured ectopic pregnancy or gastrointestinal hemorrhage, sizable quantities of blood must be available even though all may not be used. The dosage requirement involves considerable judgment. Decreased blood volume is not reflected in the hematocrit,

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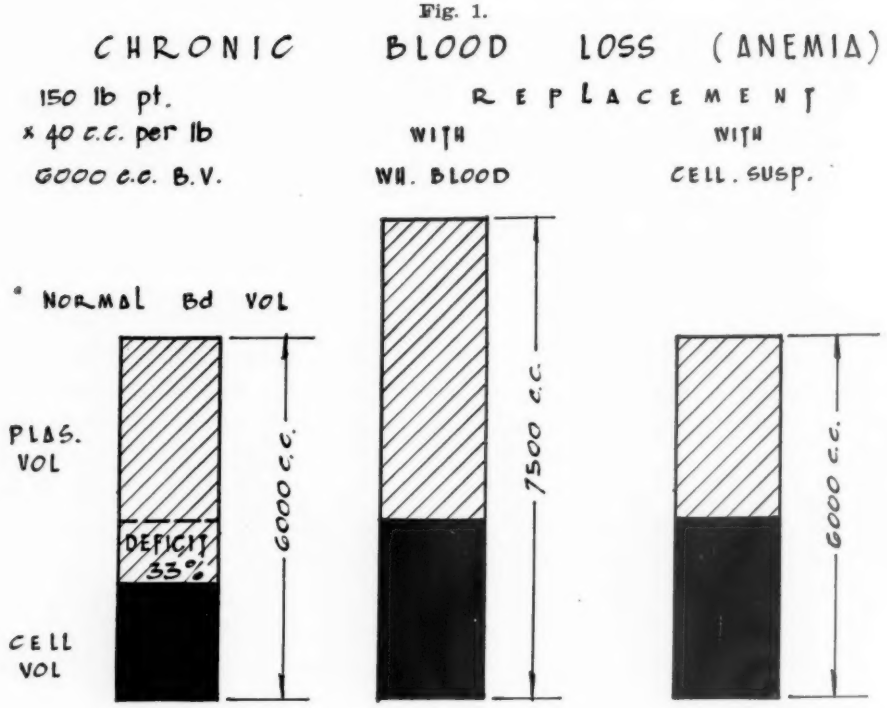
Fig. 1.



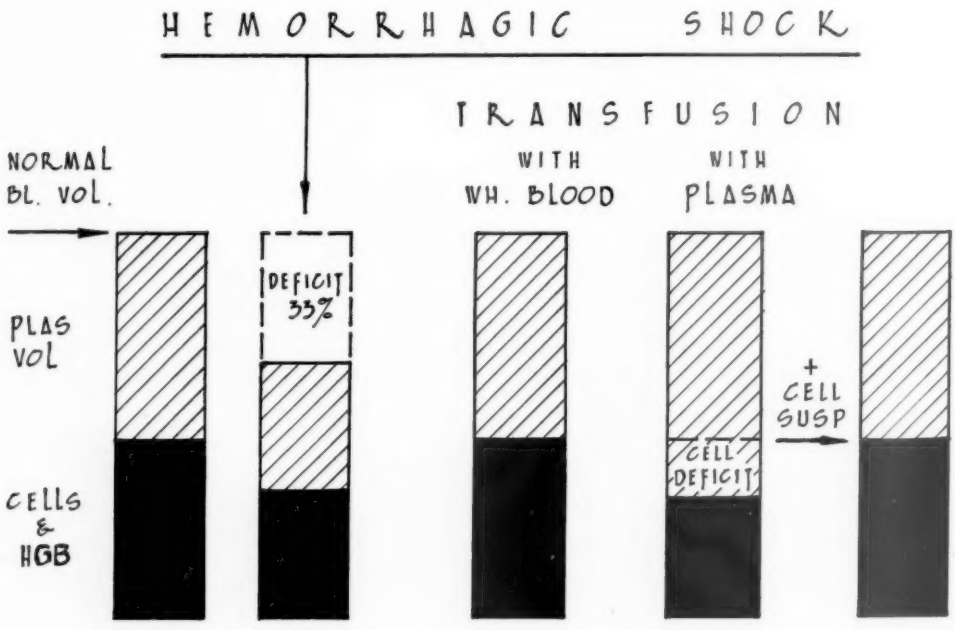
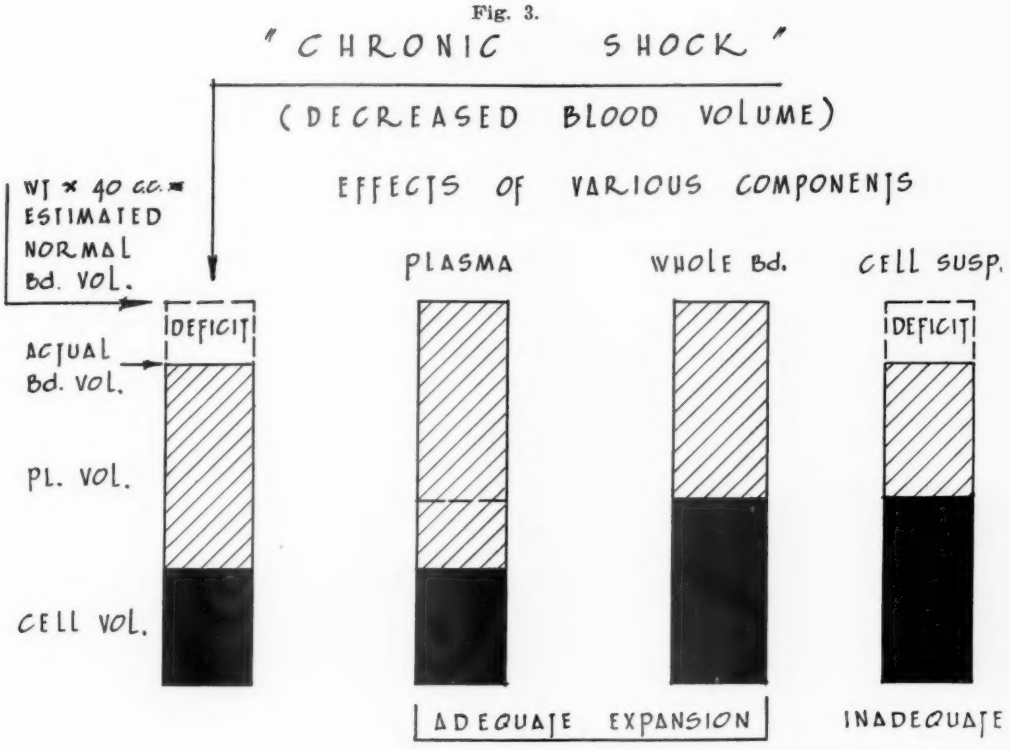


Fig. 2.

Fig. 1.—Bar 1 shows decrease of cell mass without change in blood volume. Bar 2 indicates that transfusion of whole blood is sufficient to restore normal hemoglobin or red blood cells but may overload the circulatory system. Bar 3 shows that cell suspension transfusion corrects the true deficit. The suspending fluid is not retained in significant amount and there is no dangerous increase in blood volume.

Fig. 2.—Bar 2 shows rapid loss of cells and plasma and peripheral circulatory failure due to loss of blood volume. Whole blood is transfusion of choice (Bar 3). Plasma must be given if whole blood is not immediately available (Bar 4). Having eliminated the threat of shock by restoring blood volume with plasma (Bar 4) the resulting anemia may be corrected with cell suspension transfusion (Bar 5). Cell suspension transfusions must not be used to treat shock.

Fig. 3.



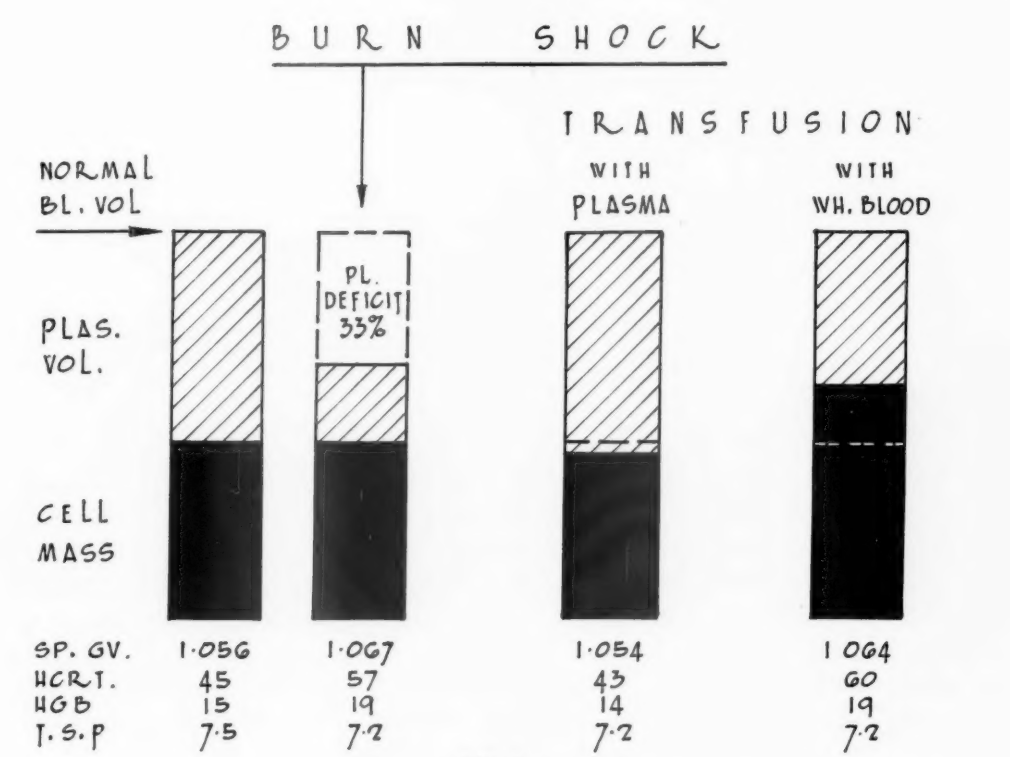


Fig. 4.

Fig. 3.—Bar 1 shows that the deficit is in cells and plasma. Administration of plasma corrects blood volume and accentuates anemia (Bar 2). Whole blood corrects deficiencies in blood volume and cell mass (Bar 3). Cell suspension transfusion may correct anemia but may fail to expand the blood volume (Bar 4).

Fig. 4.—Decrease in effective blood volume due to loss of plasma through damaged and dilated capillaries. No significant early change in red cell mass is noted (Bar 2). Restoration of blood volume with plasma is corrective (Bar 3). Whole blood may significantly increase cell mass to above normal levels which serves no useful purpose (Bar 4).

TABLE I. TRANSFUSION OF WHOLE BLOOD, RED CELLS, AND PLASMA (OCTOBER, 1948, TO OCTOBER, 1951)

	NUMBER OF TRANSFUSIONS	PER CENT OF TOTAL TRANSFUSIONS
Whole blood	70,450	71
Red cells	13,376	13.5
Liquid plasma	15,374	15.5
Total*	99,200	
Number of donors	79,200	
Number of transfusions by "phantom donors"	20,000	
Number of transfusions per donor	1.25	

*Includes pediatric patients.

hemoglobin, or erythrocyte count, as these are measurements of relative concentration rather than total amount and may be normal in a patient with known hemorrhage. Blood volume determinations with T-1824 dye and hematocrit are valuable in chronic depletion but less accurate in hemorrhage or shock. The axiom that "bleeding patients die from anoxia" suggests that hemoglobin is the prime factor. One must not forget that adequate circulation is necessary in order to oxygenate the tissues and that failure to do this is the principal cause of anoxia. Complete restoration by whole blood or plasma is the first consideration. Five or more liters may be required. Incomplete replacement on the theory that complete restoration may "blow out a clot" is dangerous. Continued shock will cause irreparable parenchymal damage. Impaired liver function may be reflected in a fall in serum albumin and globulin levels and a failure to regenerate hemoglobin. Kidney failure may result in fatal anuria. On the other hand, overenthusiastic replacement may result in a serious overload reaction, even during continued bleeding.

Another important requirement of whole blood is for replacement of loss during surgery. Estimates may be determined by using dry sponges and packs and weighing after use, or by determination of blood hemoglobin preoperatively and of hemoglobin in washings from gloves, sponges, etc., postoperatively.[1] The preoperative correction of blood volume deficits and the quantitative replacement of blood loss during surgery have almost eliminated postoperative shock.

CELL SUSPENSION TRANSFUSIONS

Red cell suspension transfusions were first introduced by Robertson[2] and their use has been encouraged by many authors.[3-6] The preparation of cell suspensions has become a simple and safe routine since introduction of the closed evacuated system of blood collection.[7] We have issued red cell transfusions at the Blood Bank of Dade County since 1941 and at the present time, with more than 3,000 transfusions issued monthly, over 400 are cell suspension transfusions.

The principal indications for red cell suspension transfusions are in the treatment of anemias which are unaccompanied by diminution of blood volume or by severe hypoproteinemia, and in patients requiring blood but in whom an increase in blood volume is contraindicated.

In the *anemia* of chronic hemorrhage associated with normal blood volume, in iron deficiency anemia, nutritional anemia, and anemia of pregnancy in the absence of toxemia, and in certain blood dyscrasias, cell suspension transfusions should be used. In these cases the plasma volume may be normal or increased[8] and this component of whole blood is unnecessary. The cell mass alone may be decreased. Even in nutritional anemia the small amount of additional protein furnished by whole blood is therapeutically ineffective. The protein content of the plasma from 500 c.c. of blood is only 19 Gm. A patient requiring 150 Gm. of protein daily would need 2,000 c.c. of plasma or eight donor units daily. To attempt to supply this amount of protein by transfusion would be wasteful and even dangerous.

In patients undergoing *elective surgery* and having an essentially normal blood volume but requiring preoperative correction of anemia, the hemoglobin and red cell deficiency may be restored to the desired level by a single large transfusion of cell suspension. Thus time is saved and the danger of an overload reaction is minimized. In such patients with marked anemia, the last one or two units required should be administered as whole blood just before or during the operation to maintain optimum blood volume and circulation as a safeguard against shock.

Red cell suspension transfusions must never be used in the treatment of shock since the osmotic pressure of the suspending fluid is negligible, and, in contrast to the retention of the plasma colloids, there is no significant retention of the crystalloids in the vascular tree. The capillaries are freely permeable to water, electrolytes, and crystalloids. Since approximately 75 per cent of the injected fluid rapidly leaves the vascular tree (as the proportion of tissue to circulating fluids is 3 to 1 and an equilibrium is established), only 25 per cent remains. Red cells exert no osmotic force in drawing or holding fluid within the vascular system. They increase the viscosity of blood but contribute nothing to the effective blood volume. Cell suspension transfusions may also be used to correct an anemia which may be disclosed following the treatment of shock with plasma.

In treating *pediatric patients,* the size of the patient and the accessibility of veins may limit the volume and number of transfusions that can be given. Cell suspension transfusions may be better tolerated and may be given in larger doses. However, in the treatment of infant diarrhea and severe infection where shock is present or impending, whole blood or plasma is required; and, of course, in exsanguination transfusions whole blood must be used.

The majority of *cardiac patients* do not tolerate sudden increases in the effective blood volume and must be guarded against overload transfusion reactions. Cell suspension transfusions are therefore much safer for these patients.

Preparation of Cell Suspension.—It is our practice to withdraw blood from donors in sodium citrate solution and then to centrifuge in order to pack the red cells and obtain a maximum yield of plasma. After plasma has been withdrawn, the red cell pack is stored in the refrigerator for no longer than five days. When cell suspension is requested the desired amount of suspending

liquid is added to the bottle containing the red cells. We use Alsever's solution for this purpose since it has a relatively low sodium content. The amount necessary for resuspending the cells of 500 c.c. of blood contains 4 Gm. of trisodium citrate, 0.25 Gm. of citric acid, 9.33 Gm. of anhydrous dextrose, and 2.09 Gm. of sodium chloride. The amount of Alsever's solution may be reduced to approximately one-half the volume of the red cell mass. This yields a suspension which can be readily given, and yet limits the total amount of fluid injected. It is, therefore, the transfusion of choice for the cardiac patient requiring correction of severe anemia.

THE DOSE OF BLOOD

It is important to determine the actual amount of blood or cell suspension required in each case and to affect a significant correction of the deficit whenever possible. This may require replacement of a large proportion of the patient's estimated blood volume or red cell mass.

The theory that small doses of blood stimulate red cell maturation is false. The apparent delay in the increased red cell count following transfusion is the result of an increase in blood volume following whole blood transfusion. If the plasma proteins are thus increased, further expansion may result by attraction of extravascular fluids and an immediate red cell count may show no rise. Final adjustment of blood volume and red cell count may not be apparent for twenty-four hours or longer.

In *calculating the dose* of whole blood or cell suspension in an individual case, one must consider the hemoglobin, erythrocyte count, and the patient's standard blood volume and cardiac and renal status. Blood volume determinations have their greatest usefulness in the quantitative correction of constricted blood volume in the preparation of protein-depleted patients for surgery. They are unnecessary in the quantitative correction of anemia without hypovolemia and will not be discussed here. The following method of determining the dose of blood and/or cell suspension has proved entirely satisfactory in our hands. This method does not apply in the presence of shock.

Normally 7.5 to 8 per cent of the body weight is blood. In marked obesity it may be less. For practical purposes 8 per cent of the patient's normal weight is used in estimating his standard blood volume. The donor unit of 500 c.c. is accepted as one pound.

Example: 8% of 1 pound (or 500 c.c.) = 40 c.c.
Standard blood volume of 150 pound patient = $150 \times 40 = 6{,}000$ c.c.

It is necessary to determine the percentage ratio between 500 c.c. and the blood volume of the patient.

Example: Weight = 150 pounds. Blood Volume = 6,000 c.c.

$$\frac{\text{Donor Unit}}{\text{Blood Volume}} = \frac{500}{6{,}000} = \frac{1}{12} = 8.3\%$$

The normal erythrocyte count or hemoglobin multiplied by this factor gives the expected increase by administering 500 c.c. of blood or cell suspension.

8.3% × 5,000,000 (R.B.C.) = 415,000 R.B.C. (anticipated increase in red blood cells per 500 c.c. donor unit)
8.3% × 100% (Hgb.) = 8.3 (increase in hemoglobin per cent per 500 c.c.)
8.3% × 15 (Gm.) = 1.24 Gm. (increase in hemoglobin per 500 c.c.)

In determining the total amount of blood or cell suspension required to bring the hemoglobin or red cell count to the desired level the patient's deficit is determined, and this is divided by the estimated increase resulting from a single 500 c.c. unit.

Example: 150 pound patient = 6,000 c.c. blood volume
500 c.c. of blood = 8.3% increase
Desired red blood cell count = 5,000,000
Actual red blood cell count = 2,500,000
Deficit = 2,500,000

$$\frac{\text{2,500,000 (deficit)}}{\text{415,000 (estimated increase 1 unit)}} = 6 \text{ (donor units) or 3,000 c.c.}$$

Example: 100 pound patient = 4,000 blood volume
Present hemoglobin 5 Gm. = deficit 10 Gm. per 100 c.c.
10% × 4,000 = 400 Gm. hemoglobin deficit

In this case a concentrated cell suspension may be furnished containing 22 Gm. of hemoglobin per 100 c.c.

$$\text{Thus: } \frac{400}{22} = \text{1,800 c.c. concentrated cell suspension required.}$$

PLASMA

The recent trend away from plasma and toward the empiric use of whole blood is not justified. The effectiveness of plasma on the battlefields during World War II and in the emergency rooms of hospitals should not be forgotten.

The incidence of homologus serum jaundice and the fear of this complication of transfusions has unduly influenced many physicians to abandon the use of plasma. It would appear from the numerous reports on incidence in various parts of the United Statese that the problem of homologous serum jaundice is a variable one. In Dade County, Florida, the incidence of jaundice following whole blood transfusion is less than 1 in 5,000 transfusions. In other areas reports have been as high as 1 per cent following whole blood transfusions. During the past five years we have issued approximately 20,000 units of liquid plasma from the Blood Bank of Dade County and have not had a case of hepatitis resulting from the injection of plasma alone. Since 15 per cent of our transfusions are issued as plasma and since each pool of plasma represents blood from six donors, we feel that these plasma recipients have been exposed to approximately the same number of donors as the recipients of whole blood. We have been able to establish definite cases of transfusion hepatitis from whole blood, but none from the use of plasma. We believe that our method of preparation of liquid plasma and its storage at room temperature for ninety days before issue accounts for the freedom from hepatitis. We are in agreement, therefore, with the observations of Garrott Allen[9] who believes that the agent of homologous serum jaundice does not survive in plasma stored at room temperature.

When plasma may be used instead of whole blood certain potential risks of transfusion reaction are minimized. With the recognition of newer blood groups this danger from whole blood increases. Hemolytic reactions are virtually unknown with plasma transfusions.

Blood plasma is in itself a very useful and complex component. Its main function is the maintenance of effective blood volume. Its principal use in transfusions, therefore, is in the treatment of shock which results whenever the effective blood volume is lowered to the extent that circulation is impaired and tissue anoxia results. A discussion of shock is not within the scope of this paper; however, a few examples of specific indications will suffice to review the value of plasma in shock.

In *hemorrhagic shock* with severe oligemia whole blood should be given. However, plasma, which can be given immediately, may be lifesaving. The time consumed in the selection of compatible whole blood may be too great in instances of severe hemorrhage. Blood plasma should be used promptly and liberally in treating these patients. If this is done, less is required, irreversible shock may be avoided, and liver, renal, and cerebral damage is less likely to result. Perhaps 30 or 40 per cent of the total blood volume may need immediate replacement. The deficit in red cells is not an immediate threat to life. Generally, anoxia is due to circulatory failure and not to anemia and may be adequately corrected by the restoration of blood volume with plasma alone. The blood cell deficit may be corrected in less haste and confusion and with less danger of reaction later, using whole blood or even cell suspension if adequate plasma has been provided to restore proper circulation. Immediately after severe hemorrhage, or during concealed hemorrhage, laboratory tests to determine blood volume or cell mass are unreliable.

When transfusion following arrested hemorrhage is delayed, the gradual expansion of plasma volume may have reached or exceeded normal.[10] Apparently such patients no longer need plasma. In these cases, on theoretical grounds and from our experience, correction of the cell mass deficit by cell suspension transfusions minimizes the burden on the cardiovascular system. With the complete restoration of plasma volume, by its administration or spontaneously from intracellular fluid,[11] the hematocrit will reveal the true degree of hemorrhage. As much as 3,000 c.c. of whole blood may be necessary to restore a 50 per cent deficit in cell mass. The resulting overexpansion of blood volume may be avoided by the use of cell suspension. This final complete restoration of plasma and cell mass is essential in order to prepare the patient for necessary surgery.

The condition referred to as *chronic shock* is characterized by a diminished blood volume. The plasma volume, cell mass, circulating and total body proteins are all decreased. This condition is usually associated with chronic infection, malignancy, and nutritional disturbances. It must be suspected and corrected, if possible, before surgery, as acute surgical shock from operation or anesthesia superimposed upon chronic shock will seriously jeopardize the life of the patient. The blood volume deficit in seriously depleted patients may exceed 1,500 c.c.

A carefully elicited history, to include weight loss, infections, draining wounds, inadequate food intake, and examination for evidence of dehydration, poor skin turgor, and other disorders, should reveal these cases. Plasma volume, circulating plasma protein, and cell mass determinations with the necessary calculations to determine deficits in each patient will give the information necessary for adequate qualitative and quantitative replacement therapy.[12] However, in the absence of these tests, 40 c.c. per pound of recent weight loss in a nonobese person may be used as a rough guide to the degree of blood volume deficiency. Patients with a deficit of 1,000 c.c. are poor surgical risks. Even a 500 c.c. deficit should be corrected preoperatively.[13] The correction should consist of replacement by whole blood, supplemented with plasma, or cell suspension to quantitatively replace both components. In many patients, plasma alone is sufficient for the restoration of the effective blood volume so necessary for emergency surgery. The associated total-body protein deficit may be great. It is approximately thirty times that of the circulating plasma protein deficit. This is a nutritional problem.[14] Neither blood nor plasma will significantly increase the plasma or tissue proteins in hypoproteinism, as the protein in the blood cells is not immediately available for utilization and that present in the plasma is only 19 Gm. per 500 c.c. of blood. Their use for this purpose alone is wasteful and dangerous. Several measures may be combined to restore tissue and plasma protein when depleted. The correction of protein deficiency by diet alone, on the other hand, will result in the gradual expansion and restoration of normal blood volume. This may take several weeks, which is too long for urgent surgery.

In *severe dehydration* as in prolonged diarrhea, intestinal obstruction, and other diseases, there is always actual or impending shock. There is a loss of plasma into the interstitial spaces and this must be replaced by plasma transfusions; otherwise, the administrations of repair solutions containing water and sodium will overload the interstitial compartment and the circulating blood volume will not be restored. The renal function, so vital in correcting dehydration, will become impaired.

In *severe infections* such as generalized peritonitis or acute empyema, the shock, when present, is associated with a great loss of plasma proteins. Plasma must be administered in addition to fluid and antibiotic therapy.

In addition to the shock-correcting property of plasma, its globulins contain substances which correct deficiencies in the clotting mechanism of hemophilia, afibrinogenemia, Dicumarol poisoning, and heparinemia. It also contains immune bodies which may be indicated in certain infectious diseases. These are labile components of plasma and the plasma must be processed from fresh blood and preserved in the frozen state.

In *severe burns* and in crush injuries where shock is always present or impending, plasma must be given to restore and maintain an effective blood volume. In the treatment of patients with extensive second and third degree burns, it is important immediately to correct the deficit in blood volume and then to maintain the normal blood volume during the forty-eight to seventy-

two hours of continuing plasmorrhage. Failure to do this will result in prolonged and perhaps irreversible shock, which is responsible for the majority of deaths from severe burns.

The immediate deficit in burn shock is plasma and this deficit should be corrected promptly. Treatment should not be delayed while awaiting whole blood. The red cells are not needed at this time. There is some early loss of red cells due to thermal action on the superficial vascular bed and by sludging and toxic destruction and later by infection. This deficit as it develops should be corrected by whole blood transfusions. Other physiologic disturbances, fluid and electrolyte deficiencies, must also be anticipated and treated. Large amounts of these substitute repair solutions must be provided and equilibrium established.[15]

In the early treatment of extensive burns, large amounts of plasma are needed. Often as much as 8 to 10 L. will be required during the first seventy-two hours. It must be remembered that plasma may be lost from the circulation continually chiefly through the capillaries into the interstitial space and also through the burned area. The normal blood volume must be restored and maintained.

Many methods have been proposed to estimate the plasma requirement in severely burned patients. Some methods proposed are based upon the severity of the burn and upon the area of surface involved but do not provide for continuing replacement. Others consider only the clinical evidence of shock as determined by changes in blood pressure and pulse rate. These observations must be made and considered but must not be entirely relied upon in the evaluation of the severity of shock. Compensatory vasoconstriction, for example, may produce a relatively normal blood volume with normal pulse rate and blood pressure for a period of time. The determination of red cell count, hematocrit, and hemoglobin are impractical due to the time required for the performance of the test. The T-1824 dye method of determining plasma volume has not been proved sufficiently accurate in shock and is too complex and time-consuming. The P-32 tagged cell method of cell mass determination is not generally available.

DETERMINATION OF PLASMA REQUIREMENT IN BURN SHOCK

We feel that the only practical method of determining the amount of plasma required is by the measurement of the plasma deficit itself, by determining the hemoconcentration of blood, and for this purpose we use the specific gravity determination by the copper sulfate method. The test is rapid and the result is immediate.

The specific gravity of blood is influenced by the concentration of its major components. It is therefore variable in anemia and hypoproteinemia. Like many other tests it is relative within limits. In a severely burned but previously well patient it is the most valuable guide to therapy and will determine variations not yet reflected in the changes in pulse or blood pressure in clinical shock.

A rack of bottles containing copper sulfate solutions of specific gravity from 1.045 to 1.075 is kept at the bedside and one-half hour or hourly determinations of whole blood specific gravity may be made using one drop of blood from

the finger tip, toe, or ear lobe. Upon falling into the solution, the drop of blood is immediately enclosed in a sac of copper proteinate and will remain suspended in the solution of equal specific gravity for ten or fifteen seconds. One test may be made for each 1 c.c. of solution, or twenty-five or thirty tests for 30 c.c. volume, without materially altering the test solution.

Normal plasma specific gravity is 1.024 to 1.027 and whole blood specific gravity is 1.050 to 1.058 with slightly higher levels in males than in females. For practical purposes 1.056 is accepted as normal for the determinations. The difference between plasma and whole blood specific gravity, approximately 0.030, is due to the weight of red cells. If we accept 90 per cent as average normal hemoglobin, a variation of 0.001 (one point) represents a variation of 3 per cent in hemoglobin or a 3 per cent hemoconcentration or hemodilution of the blood tested.

Specific gravity of normal whole blood	= 1.056	
Specific gravity of normal human plasma	1.026	
Difference—specific gravity of red cells	0.030	= 90% hemoglobin
	0.001	= 3% hemoglobin

Example: A 150 pound severely burned patient.—
150 × 40 = 6,000 c.c. standard blood volume
Specific gravity of patient's blood = 1.067
1.067 - 1.056 (normal) = .011
11 × 3 = 33 (approximately 33% hemoconcentration)
33% of 6,000 c.c. = 2,000 c.c. blood volume deficit

Following the above determinations 2,000 c.c. of plasma is administered rapidly. Just before administration is completed the specific gravity determination is repeated and the deficit is again determined, the required dosage calculated, and administration of plasma continued as indicated. If the specific gravity is found to be normal, the rate of flow may be markedly decreased or discontinued. The insertion of a plastic catheter into the vein assures an open route for continual or repeated administration of plasma and other fluids.[16] Specific gravity determinations are made every hour, and recurring hemoconcentration is again corrected throughout the critical seventy-two hours following severe burns. The oral or intravenous use of fluids and electrolytes, such as Ringer's lactate, are important in the management of these cases.

As a result of red cell loss after the first twenty-four hours, and in the treatment of severely burned patients known to be anemic, correction of shock by adequate plasma may result in a specific gravity determination well below 1.056. In such cases the presence of anemia will be recognized and one or two units of whole blood may be administered. Patients effectively treated for burn shock may develop anemia. After the danger of shock has passed, the anemia may be corrected with cell suspension transfusions. The characteristic weight loss and severe hypoproteinemia is a nutritional feeding problem and the use of plasma for this purpose is wrong.

SUMMARY

A more rational and specific use of blood transfusions is urged. The use of whole blood, cell suspension, and plasma, separately or in combinations, to meet the specific and quantitative needs is discussed.

The relative significance of the blood volume and body protein deficits in the chronically ill patient are discussed in relation to the indications and urgency of replacement requirements.

Indications and advantages of the separate blood components for transfusion are outlined and a method of quantitative replacement of these components is presented.

Cell suspension and whole blood replacement in anemia is calculated by using the percentage deficit in the patient's blood count estimated on a standard blood volume of 40 c.c. per pound of body weight.

A method of continual quantitative plasma replacement in burn shock, based upon bedside hemoconcentration determinations by the copper sulfate method, is presented. The hemoconcentration is quantitatively corrected using 40 c.c. per pound of body weight as standard blood volume. This is repeated at one- or two-hour intervals during the forty-eight or seventy-two hours of continuing plasmorrhage.

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CERVICAL INTRACAROTID PRESSURE STUDIES: THEIR SIGNIFICANCE IN THE MANAGEMENT OF INTRACRANIAL ANEURYSMS

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THE management of patients with spontaneous subarachnoid hemorrhage has always been a serious problem. With the development of percutaneous carotid angiography and its wide adoption as a diagnostic procedure, the accurate diagnosis of specific vascular anomalies as the cause of hemorrhage in these patients is now frequently made. The angiographic visualization of an intracranial aneurysm in such a patient raises the problem of the advisability of its surgical treatment. While some brilliant results have been reported by direct intracranial surgical attack on aneurysms of the circle of Willis, in general the direct intracranial procedures are so hazardous that the attention of most neurological surgeons has turned to methods of reducing pressure on the aneurysmal wall. The most obvious means of attempting to accomplish this has been carotid artery ligation.

There is no uniformity of opinion concerning the effectiveness of carotid artery ligation in preventing further episodes of subarachnoid hemorrhage. There has been no positive evidence to indicate that carotid artery ligation actually results in a decrease in pressure at the aneurysmal site on the circle of Willis. In 1948 and in 1950, Sweet and co-workers[3, 4] described a method of recording the internal carotid artery pressure during carotid occlusion, using a Sanborn electromanometer. Great credit should be given to these workers since their efforts represent the first good description of intracarotid artery pressures during occlusion of various portions of the carotid trunk. In the series of thirty-nine cases reported by Sweet and associates[4] no mention is made as to how many of the patients had intracranial aneurysms, or in how many an actual therapeutic ligation was carried out. In an attempt to investigate the practical usefulness of intracarotid pressure determinations in the treatment of intracranial aneurysms, a series of pressure determinations has been made in a group of eleven patients at the time therapeutic ligation was carried out. Each patient had an intracranial aneurysm in the region of the circle of Willis proved by cerebral angiography.

METHOD

Under local procaine anesthesia the common, internal, and external carotid arteries were exposed for the purpose of performing a therapeutic carotid liga-

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TABLE I. CERVICAL INTRACAROTID PRESSURES OBTAINED IN ELEVEN PATIENTS WITH ANEURYSMS OF THE CIRCLE OF WILLIS*

PATIENT	AGE (YEARS)	I. C.	INTERNAL CAROTID PRESSURE WITH					% DROP	REMARKS
			E. C. OCC.	C. C. OCC.	E. C. AND C. C. OCC.	E. C., C. C., AND O. C. OCC.	I. C. OCC.		
E. C.	28	120/75					72/40	40	
M. V.	33	162/112	162/112	66/60			50/45	69	Hemiplegia. Partial ligation to pressure of 100
C. F.	39	120/70	120/70	50/35	50/35	20/20		58	
H. T.	34	90/40	90/40	40/22	40/22	40/22	40/22	55	Moribund. Died in 24 hours
B. P.	20	122/85	122/85	40/40	40/40	22/22	40/40	67	
E. D.	38	150/80	150/80	40/40	40/40	20/20	40/40	73	Hemiplegia. Partial ligation followed by complete ligation in 3 weeks
T. M.	47	145/100	145/100	70/62	70/62	25/25	75/67	48	
S. S.	53	135/100	135/100	50/46	50/46	30/30	65/60	51	
B. W.	33	110/65		40/30	20/15		20/15	81	Partial ligation. Well until sudden death one week later
S. D.	41	200/130	200/130		154/140	70/70	126/112	37	Hemiplegia with occlusion of opposite carotid artery
G. B.	27	150/95	150/95	60/50	60/50		60/45	60	Hemiplegia. Partial ligation to pressure of 100

*The abbreviations used are C. C., common carotid artery; E. C., external carotid artery; I. C., internal carotid artery; O. C., opposite carotid artery; Occ., occluded carotid artery. The column labeled "% drop" indicates the percentage drop in pressure in the internal carotid artery distal to the point of occlusion of that artery.

tion. Prior to the ligation, blood pressure determinations were made by inserting a No. 18 gauge siliconized needle into the internal carotid artery. The needle was connected to a Sanborn electromanometer by a polyethylene tube filled with heparinized saline, and the pressure was recorded by an ink-writing oscillograph. The pressure in the internal carotid artery was recorded with a free flow, with the external carotid artery occluded, with the common carotid artery occluded, with the common and external carotid arteries occluded, with the common, external, and opposite carotid arteries occluded, and with the internal carotid artery occluded. Following the pressure determinations, a clamp was placed on the internal carotid artery for thirty minutes, during which time the patient was observed, and following which time the internal carotid artery was either partially or completely ligated by means of a heavy silk ligature tied over a band of fascia. Since the operative site was well infiltrated with procaine, it is believed that any effect of the carotid sinus reflex was eliminated. The blood pressure in the arm was checked frequently during the operative procedure by an anesthetist, and in no instance could any drop in the intracarotid artery pressure be attributed to a drop in the systemic blood pressure.

RESULTS

The results are summarized in Table I. With the recording needle in the internal carotid artery, the external carotid artery was occluded and, in each instance, the pressure in the internal carotid artery was found to be unchanged. The clamp was then removed from the external carotid artery, and the common carotid artery was occluded and the pressure recorded. With the common carotid artery occluded, a clamp was also placed on the external carotid artery in order to determine if this would result in a further drop in the internal carotid pressure. In every case except one, the pressure in the internal carotid artery remained the same, whether the common or the common and the external carotid arteries were occluded (Fig. 1). In one case, there was a further significant drop in the internal carotid artery pressure following occlusion of the external carotid artery. A comparison was also made of the pressure in the internal carotid artery following occlusion of the common carotid artery as compared with the pressure following occlusion of the internal carotid artery. Again, there was no significant difference except in the case previously described, where the pressure was 50 per cent lower with the external removed from the internal carotid circulation.

In seven cases the internal carotid artery pressure was measured with the common carotid and the external carotid arteries occluded, following which the opposite carotid artery was also occluded. In one case the pressure remained unchanged. In the others the pressure dropped from 50 to 60 per cent of the value just prior to occlusion (Fig. 2). This would tend to indicate that a significant portion of the collateral circulation is obtained by way of the anterior communicating artery. In fact, one patient developed a transient hemiplegia following occlusion of the opposite carotid artery for less than one minute.

Following occlusion of the internal carotid artery, the percentage drop in pressure in the eleven cases varied from 37 to 81 per cent with an average of

58 per cent. Apart from the drop in systolic pressure, there was also a decrease in the pulse pressure. Prior to occlusion of the internal carotid artery, the pulse pressures varied from 37 to 70, with an average of 52. Following occlusion of the internal carotid artery, the pulse pressures varied from 0 to 32 with an average of 10. This is an average drop in pulse pressure of 80 per cent.

DISCUSSION

The pressure determinations made on this group of patients correspond closely to those obtained by Sweet and associates. Following occlusion of the internal carotid artery, Sweet found a percentage drop in systolic pressure of 49 per cent and in pulse pressure of 69 per cent. In the group of patients reported here, the percentage drop in systolic pressure was 58 per cent and, in pulse pressure, 80 per cent. These observations indicate that a significant drop in pressure is obtained in the cervical portion of the carotid artery distal to the point of ligation.

It is obvious, of course, that from the therapeutic standpoint the important pressure is that which exists at the aneurysm on the circle of Willis. It may be as Sweet and associates[3] have suggested, that since the internal carotid gives off no branches before the ophthalmic artery, the pressure at that point will be the same as in the neck. If that is true, since a considerable drop in pressure occurs in the neck, it is possible that a decrease in pressure also occurs at the site of the intracranial aneurysm, which may be sufficient to decrease the likelihood of further rupture of the weak aneurysmal wall. At the present time one can only speculate as to the exact pressure at the aneurysm and await the development of techniques for its accurate measurement.

The significant decrease in pulse pressure may also be transmitted to the site of the aneurysm. Sweet and associates[3] have pointed out that this, too, may be of importance in preventing rupture of the aneurysm since the aneurysmal wall is not subjected to as great a rhythmic expansile force.

It has frequently been said that ligation of the common is a safer procedure than ligation of the internal carotid artery, since a collateral blood flow will occur from the external into the internal carotid artery. If such a collateral flow exists, one would expect that, if the common carotid artery is occluded, the pressure in the internal should be greater when the external carotid artery is patent than when it also is occluded. This was true in only one of the cases reported here. Similar results were found by Sweet. Only two of his patients had a higher pressure when the external carotid artery was open, and in four instances the pressure was actually lower. These figures tend to indicate that in the majority of cases there is probably not a significant collateral flow from external to internal carotid artery.

Complications Following Carotid Artery Ligation.—In 1804, John Abernethy[1] recorded the first detailed description of ligation of the common carotid artery which he had performed in 1798. The patient developed a hemiplegia and died thirty hours later. Since that time the neurological complications following carotid artery ligation have remained a problem. The most generally

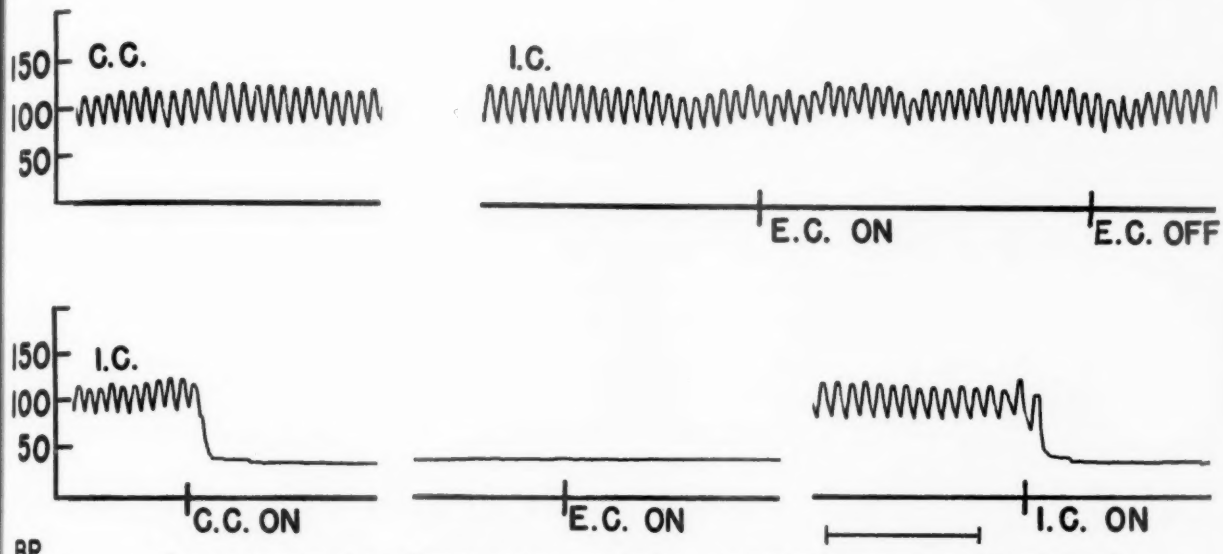

Fig. 1 (Case B. P.).—Carotid artery pressures. The ordinate represents millimeters of mercury and the horizontal line at the base represents a time interval of ten seconds. At C. C. the pressure in the common carotid artery is recorded and at I. C. the pressure in the internal carotid artery is recorded. At E. C. on, the external carotid was clamped and at E. C. off, the clamp was removed. There was no change in the internal carotid pressure during this time. At C. C. on, the pressure in the internal carotid fell from 122/85 to 40/40, a decrease in pressure of 67 per cent. Occlusion of the external carotid artery at this point did not cause any further decrease in the internal carotid pressure. The pulse pressure was too small to be measurable by the recorder. At I. C. on, the internal carotid artery was occluded with a resulting decrease in the internal carotid pressure the same as when the common carotid artery was occluded.

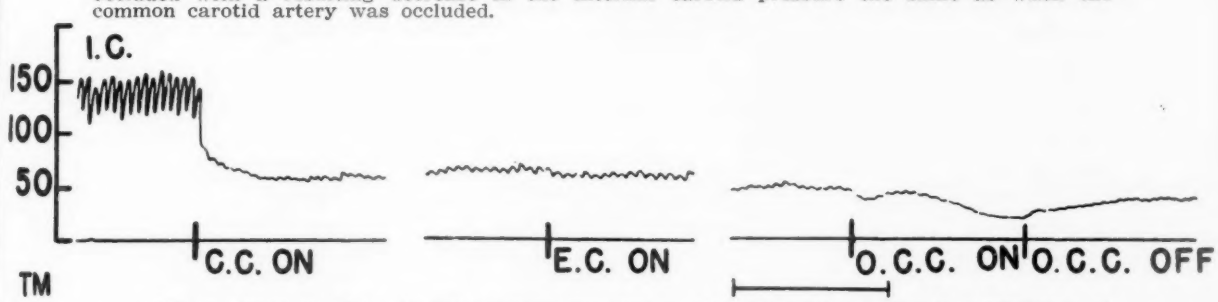

Fig. 2 (Case T. M.).—Carotid artery pressures. The ordinate represents millimeters of mercury and the horizontal line at the base represents a time interval of ten seconds. At I. C. the pressure in the internal carotid artery is recorded. At C. C. on, the common carotid artery was occluded with a resulting pressure in the internal carotid of 70/62, a decrease in pressure of about 50 per cent. When the external carotid artery was occluded at this point, there was no further decrease in the internal carotid pressure. With the common and external carotid arteries occluded, the opposite common carotid artery (O. C. C.) was also occluded. This caused the pressure in the internal carotid artery to drop from 70/62 to 25/25.

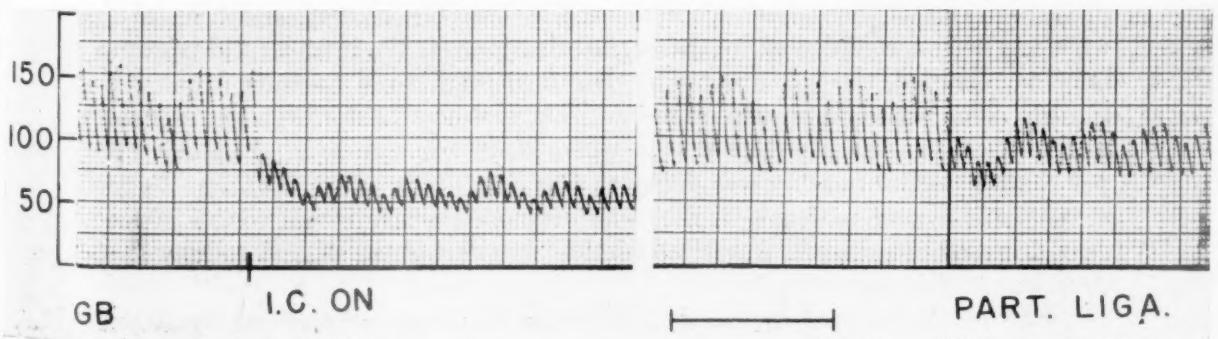

Fig. 3 (Case G. B.).—Internal carotid artery pressures. The ordinate represents millimeters of mercury and the horizontal line at the base represents a time interval of ten seconds. At I. C. on, the internal carotid artery was occluded. The pressure dropped from 150/95 to 60/50, a decrease in pressure of 60 per cent. Within ten minutes after occlusion of the internal carotid artery, the patient developed signs of a hemiplegia. Accordingly, the clamp was removed from the artery, following which the signs of hemiplegia cleared. A partial ligation of the internal carotid artery was then carried out, during which time the intracarotid pressure was being recorded. The vessel was ligated until the pressure was 100/75, a decrease in pressure of approximately 30 per cent.

accepted cause of cerebral complications is failure of the collateral circulation to compensate for the loss of the carotid blood flow.

Halsted[2] was actively interested in the problem of adequate collateral circulation following ligation of major blood vessels. In 1905 he described an aluminum band for the partial and serial occlusion of blood vessels. In his report of a case in which such a band was applied to the left internal carotid artery, he made a statement apropos of the investigations reported here: "We regretted that, in this case, the band was inadvertently rolled tighter than intended; it could, of course, have easily been removed and reapplied but our notions being rather vague as to the precise amount of constriction which we desired and being unable to determine accurately the blood pressure distal to the band, we decided to let it remain and note the results." The observations recorded in Table I show that the pressure distal to the point of ligation will give some indication as to the adequacy of the collateral cerebral circulation and thus enable one to predict the likelihood of complications.

Following occlusion of the internal carotid artery, six of the eleven patients had a drop in pressure of less than 60 per cent of the preocclusion pressure. One of these patients (H. T.), with a drop of 55 per cent, died within twenty-four hours, but she was moribund when first seen from a massive subarachnoid hemorrhage, and the operation was undertaken in view of what seemed to be an inevitable fatality.

Of the five patients who had a drop in pressure of 60 per cent or greater, three developed a hemiplegia during the thirty-minute trial period of internal carotid occlusion. This would seem to be a point of considerable practical value in deciding whether a complete or partial carotid artery ligation is indicated. Although the number of patients on whom these observations have been made is small, the difference in incidence of hemiplegia in these two groups is striking enough so that at the present time the policy has been adopted of performing carotid ligation in stages in those patients who have a drop in pressure greater than 60 per cent distal to the point of occlusion of the internal carotid artery.

In performing a partial ligation, the surgeon can usually rely only on his judgment in estimating how much of the blood flow has been obliterated by the ligature. This is somewhat unsatisfactory because one cannot be certain as to what has been accomplished by the partial ligation. If the intracarotid pressure is being recorded, the ligature can be tied until the desired pressure drop is obtained. This was done in two of the patients in whom partial ligation was carried out. In one patient (M. V.), in whom there was a drop in pressure of 69 per cent, a partial ligation was performed so that the pressure drop was 38 per cent. In a second patient (G. B.), who developed a hemiplegia with a 60 per cent decrease in pressure, a partial ligation was performed so that the pressure drop was 33 per cent (Fig. 3).

The relationship of the cervical intracarotid artery pressure at the site of the aneurysm is of importance in considering the likelihood of further episodes of bleeding. While these observations have also emphasized the relationship of the cervical intracarotid artery pressure to the development of hemiplegia, it should be remembered that in this particular instance the pressure per se is

only of significance in its relation to cerebral blood flow. The maintenance of an adequate cerebral blood flow is necessary in order to prevent hemiplegia following carotid ligation. There are factors, other than the blood pressure, involved in the determination of an adequate cerebral blood flow. The results obtained in these patients, however, seem to indicate that in lieu of the actual determination of cerebral blood flow, the intracarotid artery pressure is an excellent indication as to the adequacy of the cerebral blood flow following carotid ligation.

SUMMARY

In a group of eleven patients with aneurysms of the circle of Willis, pressure determinations of the internal carotid artery in the neck were made during occlusion of various portions of the carotid trunk. During occlusion of the internal carotid artery, the average drop in systolic pressure was 58 per cent and the average decrease in pulse pressure was 80 per cent. This may be an indication that ligation of the carotid artery in the neck may result in a therapeutic decrease in pressure at the aneurysmal site on the circle of Willis.

Hemiplegia did not occur if the decrease in pressure was less than 60 per cent, whereas it did occur in three out of five patients with a drop in pressure of 60 per cent or more. A partial ligation is probably indicated in patients whose pressure drop is 60 per cent or greater. The recording of the carotid pressure during partial ligation provides the surgeon with an accurate method of determining how much the carotid circulation has been decreased by the partial ligation.

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THE TRANSVERSE INCISION IN PHARYNGEAL PULSION DIVERTICULA

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INTRODUCTION

SINCE 1884[1] when surgery was first utilized in the treatment of pharyngeal pulsion diverticula, the vertical incision has been the avenue of approach. This incision, with very little modification, has extended from the suprasternal notch to the level of the hyoid bone along the anterior border of the left sternocleidomastoid muscle. On rare occasions the surgeon would deliberately choose the right side of the neck when clinical and x-ray findings so indicated. The surgical procedures performed through this incision are the one- or two-stage excisions of the sac, inversion of the pouch, and diverticulopexy.

Invariably the upper limit of the dissection is at the level of the lower border of the cricoid, whereas, regardless of the size of the diverticulum, the lower extent of the dissection is limited by the presence of the sternoclavicular joint. Any sac extending into the superior mediastinum posteriorly is beyond visual delineation regardless of how much the vertical incision is extended downward. Therefore, the zone between the cricoid and suprasternal notch is the extent of the vertical exposure attained in this type of surgery. Laterally the sternocleidomastoid must be markedly retracted while the head is rotated to the opposite side. Medially the midline cervical viscera must be sharply rotated to the right in order to force the esophagus with its diverticulum to the left into the open space made by retracting the sternocleidomastoid laterally. The lateral retraction of the carotid sheath and its content is of less importance because it lies at a deeper level than the esophagus. It is in the transverse diameter of this surgical field that the vertical incision proves to be a handicap. The skin acts as a limiting brake to the lateral retraction of the sternocleidomastoid muscle and medially the neck viscera must be rotated against this vertical barrier, all of which is greatly exaggerated when the head, in addition, is rotated to the right.

TECHNIQUE

With the preceding factors in mind, we evaluated the usual left vertical approach to a pharyngeal pulsion diverticulum in a 55-year-old woman. In this patient, the sac extended down to the mediastinal inlet and seemed to be in the usual midline position on x-ray examination. However, clinically, pressure to the right of the cricoid elicited a distinct gurgling sound which was not obtained on the left side. The patient also had a very short, fat neck, which usually further complicates the ease of exposure. We decided, therefore, to approach this lesion through the usual thyroid collar incision, primarily because

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we wished to be in a position to shift from the left to the right side, if necessary, without the compulsion of making two separate and cosmetically undesirable, long, vertical neck incisions. We were favorably impressed with the excellent exposure obtained.

The incision (Fig. 1) which was 2 cm. above the clavicle was carried to about 3 cm. lateral to the posterior border of the left sternocleidomastoid muscle and to about 3 cm. to the right of the midline. The diverticulum (Figs. 2*A* and 2*B*) was easily visualized on the left side, and the gurgling on the right side was found to be due to a widening of the fundus of the sac in that direction. The vertical exposure between the suprasternal notch and the upper border of the thyroid cartilage was easily maintained by temporarily suturing the upper and lower skin flaps to the drapes. The transverse extent of the surgical field was particularly satisfying because the collar incision removed the skin barriers associated with the vertical incision. Thus we were able to more readily and sufficiently retract the sternocleidomastoid muscle while the neck viscera could then be rotated easily to the right, almost ninety degrees, bringing the neck of the diverticulum into complete view (Figs. 3*A* and 3*B*). This latter was possible, also, because the neck viscera could be grasped directly without having to do so through the skin, as is the case with a vertical incision.

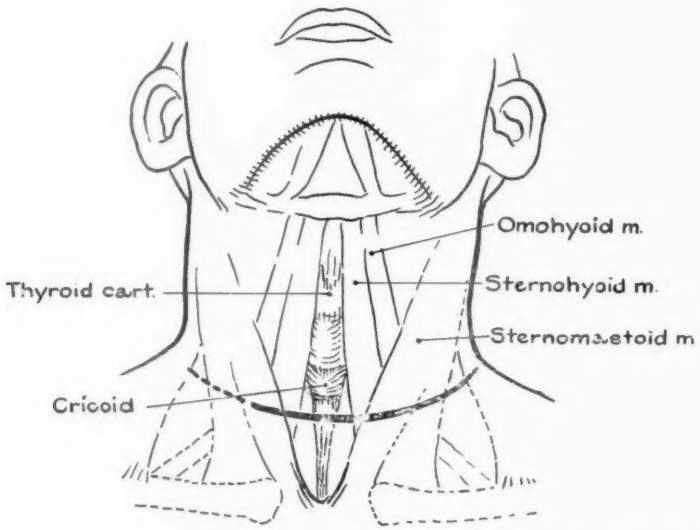

Fig. 1.—The transverse incision at the level of the cricoid cartilage with lines of extension dotted in.

Further appreciation of the value of this incision was realized when digital exploration of the superior mediastinum in this case revealed a 4 cm. firm, rounded mass contiguous to and below the lower pole of the right lobe of the thyroid. This was not palpable clinically. Accordingly, the right end of the collar incision was extended several centimeters which permitted easy delivery of the mass. It proved to be a sequestrated superior mediastinal thyroid adenoma (Fig. 4). We have since used this incision in four other cases with similar satisfactory results.

Fig. 2*A*.—Surgical field revealing the extent of both the transverse and vertical exposure through the collar-type incision. The diverticulum lies in plain view posterior to the esophagus and deep to the inferior thyroid artery.

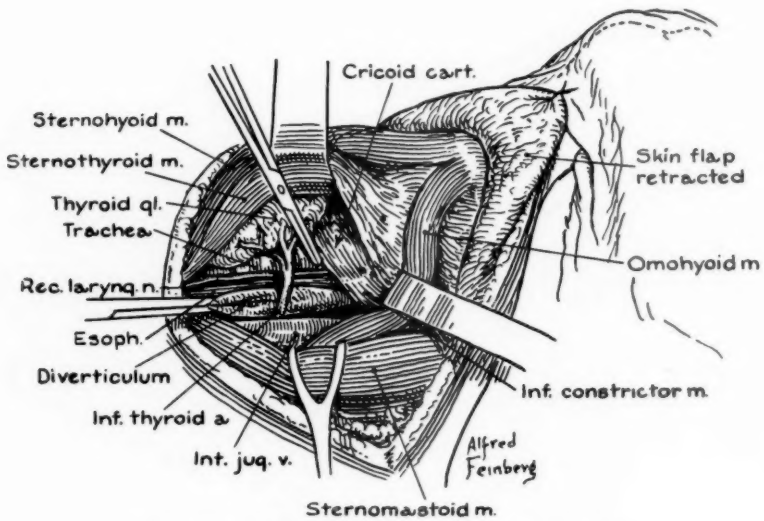

Fig. 2*B*.—Diagrammatic drawing of Fig. 2*A*.

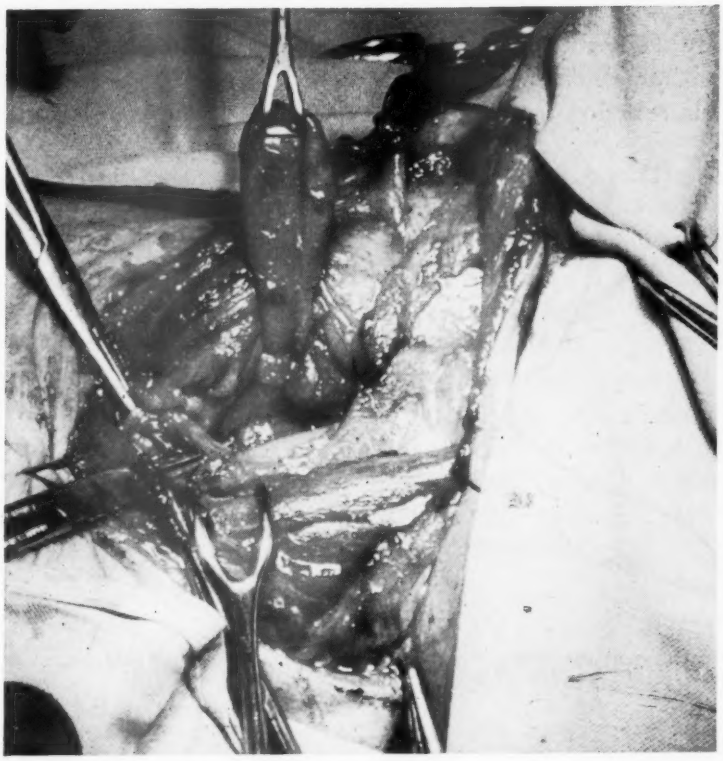

Fig. 3*A*.—Demonstration of the satisfactory exposure of the surgical field during the freeing of the diverticulum. Note the limited manual retraction required. The recurrent laryngeal nerve is in full view and separated from the neck of the diverticulum by the full thickness of the esophagus.

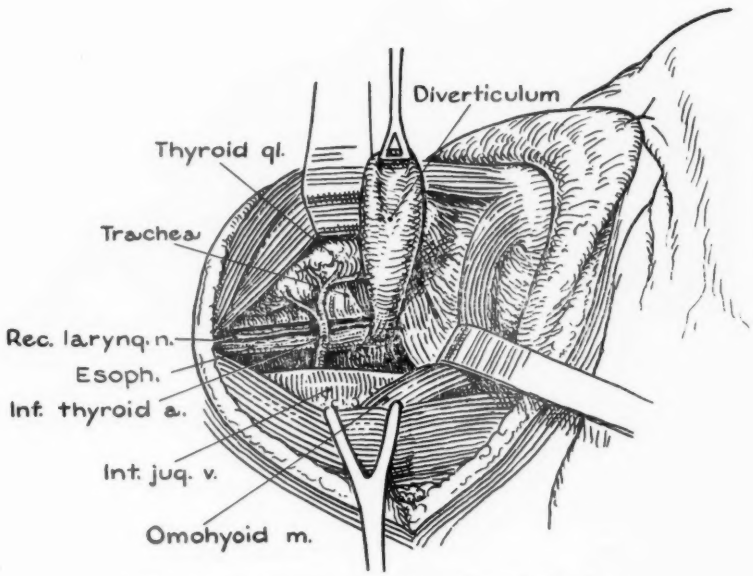

Fig. 3*B*.—Diagrammatic drawing of Fig. 3*A*.

DISCUSSION

We do not wish to imply that this is a new approach to pharyngeal diverticula. In fact, Sir Thomas Dunhill[2] reported his use of this approach since 1931. In addition, Dinsmore,[3] in 1942, and Morley,[4] in 1945, likewise described their favorable reaction to the use of the collar incision in this type of surgery.

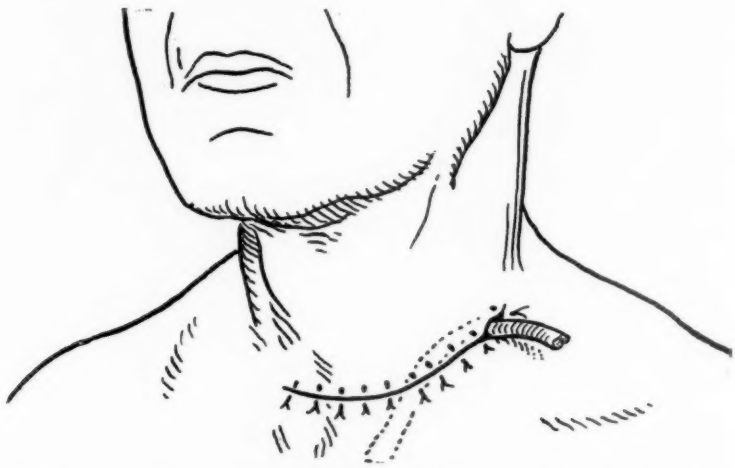

Fig. 4.—Closure showing the drain directed toward the superior mediastinum and away from the pharyngo-esophageal suture line.

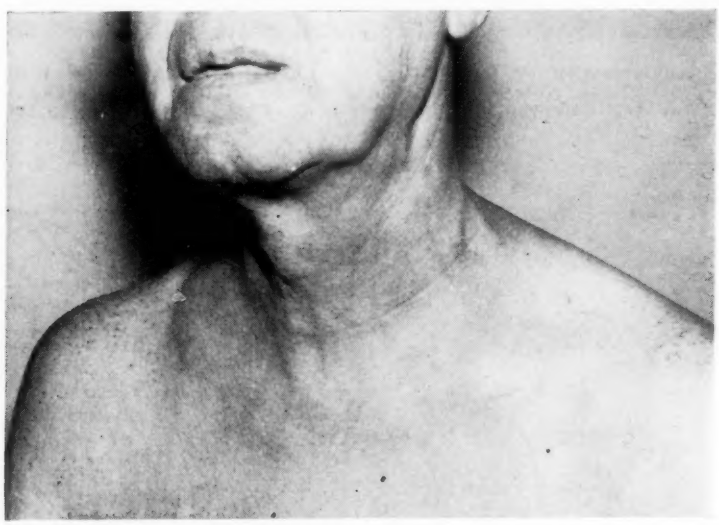

Fig. 5.—Two months postoperative; satisfactory cosmetic result.

We are certain that many other surgeons have utilized this approach. Undoubtedly all surgeons during the performance of thyroid surgery have realized the ease with which the inferior border of the cricoid, posteriorly, can be visualized in their field. In fact, tracing the recurrent laryngeal nerve to the point where it disappears beneath the lower border of the inferior constrictor muscle brings one exactly above the side of the neck of the pharyngeal

diverticulum. In view of the fact that the authors[5-10] of the analyses of many large series of cases of pharyngeal pulsion diverticula have only emphasized the use of the vertical incision, we were prompted to report our very limited but highly satisfying experience with the transverse, collar-type incision.

CONCLUSION

We believe the transverse collar incision is the preferred approach in surgery for pharyngeal pulsion diverticula. It results in better exposure because of the improvement in the transverse diameter of the field, whereas the up-and-down extent is equal to that obtained with the vertical incision. The viscera of the neck can more easily be rotated in order to bring the neck of the sac into the open surgical field. In cases of miscalculation as to the side of presentation of the diverticulum, or in those rare cases of double bilateral diverticula, the collar incision can be readily extended to the other side, avoiding the making of a second vertical incision in the opposite neck. As demonstrated in one of our cases, lesions of the thyroid can be managed through the same incision. Finally, the superior cosmetic result (Fig. 5) of the collar incision as compared to a vertical incision in the neck is a well-accepted fact.

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THE EFFECT OF HYALURONIDASE ON EXPERIMENTAL EXOPHTHALMOS

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THE "Endocrine Age" in medical research has increased our understanding of many clinically well-recognized but poorly understood entities. One of these is exophthalmos.

Over twenty years ago J. A. Schockaert produced exophthalmos in experimental animals by injections of anterior pituitary extract. Since that time Marine and Rosen, Smelser, Aird, Dobyns, Thomas, and numerous other workers have repeated and extended the ramifications of his observations.

HISTORY

Marine and Rosen[1] produced exophthalmos in thyroidectomized guinea pigs following the administration of thyrotropic substance of anterior pituitary extract. Their hypothesis of the mechanism of action was that it occurred through the hypothalamic centers via the sympathetic system.

Smelser[2, 3] produced exophthalmos in 23 of 26 guinea pigs by removal of the left cervical sympathetic ganglia. Post-mortem studies revealed a 100 per cent increase in retrobulbar fat and connective tissue, a 40 per cent increase in the weight of the dorsal lachrimal gland, and a 22 per cent increase in the volume of the extraocular muscles. He concluded that the exophthalmos was due to (A) an increase of orbital tissue, (B) edema of the retrobulbar connective tissue, fat, and muscles, (C) infiltration of these soft tissues with wandering cells, and (D) enlargement of the extraocular muscles, although muscle fiber degeneration was not striking. He found similar changes in the exophthalmos of both hyper- and hypothyroid patients.

Paulson[4] observed no marked difference in the exophthalmos that developed spontaneously in thyroidectomized animals as compared to thyrotropin-induced exophthalmos in intact animals.

Aird[5, 6] produced a more pronounced exophthalmos in guinea pigs injected with a highly purified anterior lobe thyrotropic extract than with whole anterior lobe extract, as measured by his "Camera lucida principle." He systematically ruled out the adrenals and gonads as factors in producing experimental exophthalmos.

Earlier, Friedgood[7] had suggested that the experimentally induced exophthalmos was due to decreased function of the thyroid gland, which favored the development of the exophthalmos and the subsequent changes in the orbit, which

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were reversible only for a limited time. He suggested that, by avoiding the hypothyroid state, one prevented exophthalmos.

Mulvaney,[8] in a study of 2,000 cases, observed that weakness of the quadriceps muscles correlated directly with the presence of exophthalmos.

Dobyns[9] observed depletion of the depot fat and its replacement by an edematous, translucent, fibroblastic connective tissue in Antuitrin T-treated guinea pigs. He also commented on the profound myasthenia in the animals shortly after the administration of Antuitrin T.

Thomas[10] reiterated the histologic characteristics of exophthalmos, namely, increased orbital fat, edema of the normal orbital contents, congestion of the orbital vascular bed, and relaxation and hypertrophy of the extraocular eye muscles. He stated that endocrine exophthalmos follows thyroidectomy, increase in TSH (Thyroid-Stimulating Hormone of pituitary gland), or a deficiency in iodine.

Ludwig and associates[11] concluded from studies of hyaluronidase-digested sections of retroorbital tissue of exophthalmic animals that the exophthalmos induced in the guinea pig is dependent on the accumulation of large amounts of intercellular ground substance and water in the connective tissue of the orbital contents.

PURPOSE

A series of studies was designed to evaluate the role of water retention by the retrobulbar tissues in the pathogenesis of exophthalmos and to determine the effectiveness of hyaluronidase as a means of reversing the process.

HYALURONIDASE

Hyaluronidase is an enzyme with the property of hydrolyzing hyaluronic acid, a mucopolysaccharide, which is a determinant of hydrophilic properties of the intercellular ground substance and the barrier role of the ground substance between cells. Watson[12] reported increased amounts of hyaluronic acid in the subcutaneous tissue of localized myxedema. Mills and Forsey[13] and Grais[14] have induced involution of the nodules of pretibial myxedema by the local injection of hyaluronidase.

The clinical and pathologic similarity of localized myxedema and exophthalmos has been remarked upon by numerous workers.

The most popular clinical application of hyaluronidase has been to promote absorption in hypodermoclysis and in regional anesthesia. Atkinson[15] and Key[16] added hyaluronidase to the procaine solution used in cataract and other eye surgery and found that it permitted the use of smaller volumes of the local anesthetic. It had no damaging effect on the pupil, and the mechanical proptosis quickly subsided.

METHOD

Three guinea pigs were utilized for the first study. One was untreated, and each of the other 2 received 10 mg. of purified beef thyrotropin* daily by

*Beef thyrotropin was furnished through the courtesy of Dr. Sanford L. Steelman, The Armour Laboratories, Chicago, Ill.

subcutaneous injection for a total of 51 days. Though numerous methods have been designed for measuring the degree of proptosis, it was concluded that the changes induced would have to be sufficiently pronounced to be evident in simple photographs in order to be significant.

After each of the 3 guinea pigs received a total of 510 mg. of thyrotropin, the lateral conjunctiva was cocainized and 55.8 units of hyaluronidase* in 0.2 c.c. of sterile water was injected into the left retrobulbar space. Photographs were taken with a stop watch, and the time interval and change in proptosis were recorded. The right eye served as a control. Two days later the experiment was repeated and 350 units of hyaluronidase in 0.3 c.c. of sterile water was injected into the left retrobulbar space.

The second study utilized 2 thyroidectomized guinea pigs. Starting 2 weeks after thyroidectomy, subcutaneous injections of 10 mg. of thyrotropic hormone was given for 42 days. Twelve days after the injections were completed, 500 units of hyaluronidase in 0.2 c.c. of sterile water was injected into one eye of each animal following local cocainization of the conjunctiva. The opposite eye was used as a control.

RESULTS

The injection of the hyaluronidase solution caused an immediate mechanical proptosis due to the volume of fluid introduced into the retrobulbar space. In each experiment this resolved within 10 to 20 minutes and was followed by a relative enophthalmos as the following account shows:

First Series

Experiment I.—

Nonthyroidectomized guinea pigs: Two guinea pigs were injected with 510 mg. of thyrotropin subcutaneously over a 51-day period. Definite bilateral exophthalmos was observed in both pigs on the twenty-seventh day of treatment (270 mg.). It increased progressively.

One animal was untreated.

Fifty-five units of hyaluronidase in 0.2 c.c. of sterile water was injected into the left retrobulbar space of each animal.

Control pig (untreated): Immediate mechanical proptosis followed left retrobulbar injection of hyaluronidase solution. It resolved in 20 minutes. No enophthalmos was observed.

Black guinea pig: The following developments were observed:
Immediate mechanical bulging of the left eyeball.
Relative left enophthalmos detectable in 12 minutes.
Maximal left enophthalmos detectable in 18 minutes.
Bilateral exophthalmos to preinjection degree in 29 minutes.

White guinea pig: The following developments were observed:
Immediate mechanical bulging of the left eyeball.
Relative left enophthalmos detectable in 15 minutes.
Maximal left enophthalmos detectable in 25 minutes.
Bilateral exophthalmos to preinjection degree in 41 minutes.

Experiment II.—The second experiment was performed 2 days after Experiment I.

One hundred and fifty units of hyaluronidase in 0.3 c.c. of sterile water was injected into the left retrobulbar space of the control pig and the black guinea pig.

*Beef testis hyaluronidase (Alidase) was furnished through the courtesy of Dr. Irwin C. Winter, Director of Clinical Research, G. D. Searle & Company, Skokie, Ill.

Three hundred and fifty units of hyaluronidase in 0.3 c.c. of sterile water was injected into the left retrobulbar space of the white guinea pig.

Control pig (untreated): There occurred immediate mechanical proptosis of the left eyeball, which resolved in 19 minutes.

No enophthalmos was observed.

Black guinea pig (150 units): The following developments were observed:
Immediate mechanical bulging of the left eyeball.
Relative enophthalmos detectable in 14.5 minutes.
Maximal left enophthalmos detectable in 2 hours and 46 minutes.
Bilateral exophthalmos to preinjection degree in 3 hours and 42 minutes.

White guinea pig (350 units): The following developments were observed:
Immediate mechanical bulging of the left eyeball.
Relative left enophthalmos detectable in 13.5 minutes.
Maximal left enophthalmos detectable in 35 minutes, which persisted to 3 hours and 45 minutes.
Relative left enophthalmos still detectable after 24 hours.
Bilateral exophthalmos to preinjection degree in 26 hours.

Second Series

Two Totally Thyroidectomized Guinea Pigs.—

Beginning 2 weeks postoperatively the animals were injected with 10 mg. of thyrotropin daily over a 42-day period. A questionable slight exophthalmos was noted 13 days after thyroidectomy and 1 day prior to the onset of thyrotropic injections in the white pig. Marked exophthalmos was present 30 days after thyroidectomy and 16 days after each pig had received a total of 160 mg., which progressively increased with the continued administration of TSH to 42 days (Fig. 1).

Five hundred units of hyaluronidase in 0.2 c.c. of sterile water was injected into the left retrobulbar space of the white pig and into the right retrobulbar space of the brown pig.

White guinea pig (500 units): The following developments were observed:
Immediate mechanical proptosis of the left eyeball (Fig. 2.).
Relative left enophthalmos detectable in 29.5 minutes.
Maximal left enophthalmos detectable in 3.5 hours (Fig. 3).
Relative left enophthalmos still detectable after 22.5 hours (Fig. 4).
Bilateral exophthalmos to the preinjection degree in 26 hours.

Brown guinea pig (500 units): The following developments were observed:
Immediate mechanical bulging of the right eyeball.
Relative right enophthalmos detectable in 39 minutes.
Maximal right enophthalmos detectable in 4 hours and 20 minutes.
Relative right enophthalmos still detectable after 16 hours.
Bilateral exophthalmos to the preinjection degree in 23 hours.

DISCUSSION

Paulson, Friedgood, and Mulvaney have suggested a relationship between clinical localized myxedema and experimental exophthalmos.

Ludwig and associates, by hyaluronidase digestion in vitro, have established that increased water retention by the retrobulbar tissues in exophthalmos, as reported by Smelser and others, is dependent on the hydrophilic mucopolysaccharides, consisting largely of hyaluronic acid.

Clinical usage has proved hyaluronidase to be nontoxic. The local injection of this material in eye surgery confirms its harmless nature. It is an

enzyme that specifically hydrolyzes hyaluronic acid, decreasing the water-holding ability of the ground substance. Mills, Forsay, and Grais have effected good clinical results with hyaluronidase injections into localized areas of myxedema.

The observations herein reported extend those of Ludwig and establish the role of water retention by the retrobulbar tissues as the basis for the exophthalmos induced in experimental animals by TSH. The mechanism which induces the changes in the retrobulbar tissues is independent of the thyroid since the exophthalmos induced in thyroidectomized guinea pigs responds identically, though somewhat more slowly, as compared to nonthyroidectomized animals.

Fig. 1.

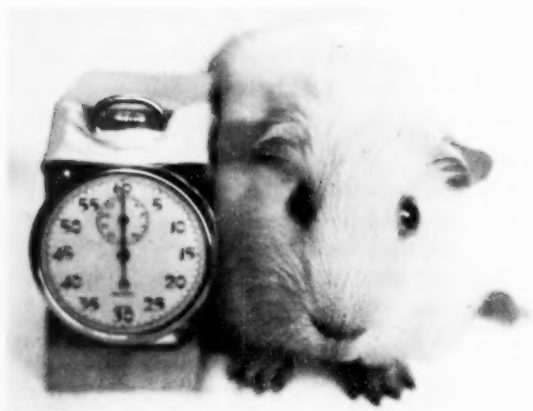

Fig. 2.

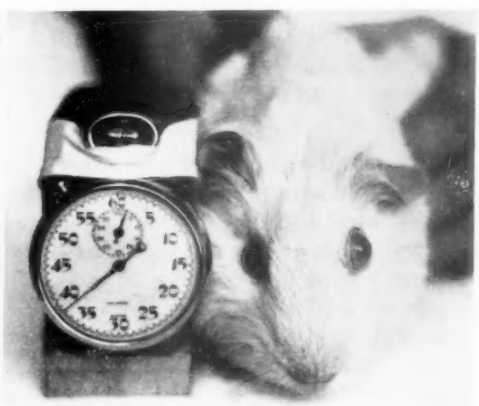

Fig. 3.

Fig. 4.

Fig. 1.—Thyroidectomized guinea pig after treatment with 420 mg. of TSH.

Fig. 2.—Same animal as in Fig. 1 with immediate mechanical bulging of left eyeball following injection of 500 units of hyaluronidase in 0.2 c.c. of sterile water.

Fig. 3.—Same animal as in Fig. 1 with relative left enophthalmos 3.5 hours after injection of 500 units of hyaluronidase.

Fig. 4.—Same animal as in Fig. 1 with return of bilateral exophthalmos to preinjection degree after 25.5 hours.

The retrobulbar injection of hyaluronidase caused no enophthalmos in the control animal. Therefore, it may be further assumed that the retrobulbar tissue of the normal animal is different from the TSH-treated pigs with respect to its water content and water-holding properties.

In view of these findings, it can be predicted that the retrobulbar injection of hyaluronidase can be made safely and that if adequate amounts of the enzyme are injected, clinical exophthalmos can be temporarily controlled.

SUMMARY

1. No gross difference in the degree or duration of exophthalmos was observed between the TSH-treated intact and TSH-treated thyroidectomized guinea pigs, but precise measurements were not made.

2. Exophthalmos was converted to enophthalmos in both nonthyroidectomized and totally thyroidectomized animals by the retrobulbar injection of varying amounts of hyaluronidase.

3. The duration of the enophthalmos induced was proportional to the amount of hyaluronidase injected.

4. Enophthalmos induced in thyroidectomized guinea pigs developed more slowly even with higher doses of hyaluronidase than in the nonthyroidectomized animals.

5. Enophthalmos was not induced in a control guinea pig following the retrobulbar injection of hyaluronidase.

6. The completely nontoxic character of hyaluronidase suggests its clinical trial in the management of clinical exophthalmos though the transient effect detracts from its usefulness.

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Case Reports

CAVERNOUS HEMANGIOMA OF THE MEDIASTINUM

Report of a Case

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HEMANGIOMA of the mediastinum is a rare tumor. In 1944 Adams and Bloch[1] reported a case of successful removal of a large hemangioma from the anterior mediastinum. A review of the literature by these authors uncovered only one previous case report which was by Winkelbauer[2] in 1929, in which a malignant hemangioendothelioma was removed from the mediastinum of a male patient. In a comprehensive search of the available literature on mediastinal tumors in 1949, Seybold, McDonald, Clagett and Harrington[3] encountered fourteen cases which satisfied their criteria for classification as mediastinal tumors of blood vascular origin. They added three cases of their own encountered among approximately two hundred mediastinal tumors treated surgically at the Mayo Clinic prior to Jan. 1, 1947. In 1950, Thomas and Chesser[4] reported the successful removal of a large benign cavernous hemangioma from the mediastinum of a young girl, 18 years of age. Horst and Beatty[5] in 1951 added a report of a successful surgical extirpation of a benign mediastinal hemangiofibroma. As near as can be determined, nineteen mediastinal tumors of blood vascular origin have been reported in the literature to date. Of the entire group of nineteen patients surgical removal of the tumor was accomplished in eight instances.

The following case is reported because of the rarity of the lesion and the unusual surgical considerations involved in the management of this particular tumor.

CASE REPORT*

A. M., a 38-year-old white female patient, was admitted to Christ Hospital on Jan. 24, 1952, with a history of having been in good health until Dec. 7, 1951, at which time she first experienced sudden shortness of breath and pain in the left anterior chest which occasionally extended into the left arm. There was no history of cough, hemoptysis, purulent sputum, dysphagia, or weight loss. Roentgenograms of the chest and fluoroscopic examination revealed a mass in the vicinity of the left hilum which did not pulsate. The patient received approximately four roentgen radiation treatments over the mediastinum without any improvement in her symptoms.

Physical examination revealed no significant abnormalities. The blood pressure was 130/75 in both arms with the patient upright. The pulses in both upper extremities were regular and of good volume. No masses were palpated in the neck, axillae, or chest. There was no distention of the cervical or arm veins.

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*The author is indebted to Dr. Raymond W. Martz for permission to publish this case report.

Laboratory studies including complete blood cell counts and urinalysis were within normal limits, except for a mild anemia manifested by a red blood count of 3.99 million and a hemoglobin content of the blood of 12 Gm. or 77 per cent.

Roentgenograms of the chest, posteroanterior and lateral projections (Figs. 1 and 2), revealed a mass approximately 8 by 5 cm. in diameter which was difficult to delineate at the level of D_3 to D_5. Fluoroscopically no pulsations were encountered in the mass. Also, at the time of fluoroscopy it was difficult to outline the ascending aorta, and it was the impression of the roentgenologist that the lesion was most probably a dilated aorta or anuerysm. A tumor mass could not be definitely excluded. Barium esophagogram showed very slight posterior deviation of the esophagus at the level of the arch of the aorta. There was no displacement of the trachea.

Bronchoscopic and esophagoscopic examinations performed on Jan. 25, 1952, revealed entirely normal findings. Tracheobronchial washings were reported positive for tumor cells and negative for acid-fast organisms.

Because of the equivocal fluoroscopic findings of an indistinct, difficult-to-outline density in the left paramediastinum and the report of tumor cells in the tracheobronchial washings, angiocardiographic studies were thought to be indicated to differentiate between aneurysm of the aorta and primary bronchiogenic carcinoma.

Second Hospital Admission.—The patient was readmitted to Christ Hospital on Feb. 17, 1952, at which time repeat posteroanterior and left lateral projection roentgenograms of the chest showed the density in the left paramediastinum to be unchanged in size or configuration.

An angiocardiogram made on Feb. 19, 1952 (Fig. 3), showed the mass to be definitely extravascular in origin. Although a mediastinal tumor was considered to be a definite possibility, primary malignant lung tumor became the first consideration because of the character of the tumor cells reported in the tracheobronchial washings.

Operation (Feb. 22, 1952).—With the patient in face-down position, the left chest was entered through the bed of the sixth rib which was resected subperiosteally. The lung was very slightly adherent to the chest wall by numerous broad-band adhesions which were divided by sharp dissection. The left lung was entirely normal. Occupying the anterior superior mediastinum was a large, gray, well-encapsulated tumor mass measuring 12 by 8 cm. in diameter. The tumor was intimately adherent to the pericardium and after being freed from this structure by sharp dissection was seen to extend up into the anterior mediastinum where it was attached to the aorta and great vessels. Additional dissection showed that the tumor extended across the midline and complete removal would be impossible with the patient in a prone position. In the course of the dissection a large vein measuring 1 cm. in diameter was seen to extend between the superior pole of the tumor and what appeared to be the left innominate vein. Because of the poor accessibility of the anterior superior mediastinum with the patient in the prone position a decision was made to discontinue the operation at this point and re-explore the patient's chest at a subsequent date by dividing the sternum anteriorly. Before closing the chest the lower pole of the tumor mass, which had the gross appearance of thyroid or thymic tissue, was amputated for biopsy studies. The cut surface of the tumor bled vigorously and was controlled with a running mattress suture of 00 chromic catgut and Oxycel gauze held in place with several interrupted sutures of the same material.

The biopsy specimen was reported by the pathologist to be made up of fibrofatty tissue containing numerous septa. The septa in several sections contained occasional lymphocytes and histiocytes.

Diagnosis.—The diagnosis was chronic inflammation with no evidence of neoplasm in tissue made up of fibrous and fatty elements.

The postoperative course was complicated by the development of total atelectasis of the left lung treated by bronchoscopic aspiration on the patient's second postoperative day. On the third postoperative day it was obvious that the patient was developing fluid in the left chest and thoracentesis yielded 300 c.c. of old blood. Roentgenograms of the chest showed an additional quantity of fluid to remain in the left chest which could not be removed by thoracentesis and a diagnosis of clotted hemothorax was made. One hundred thousand units

Fig. 1.

Fig. 2.

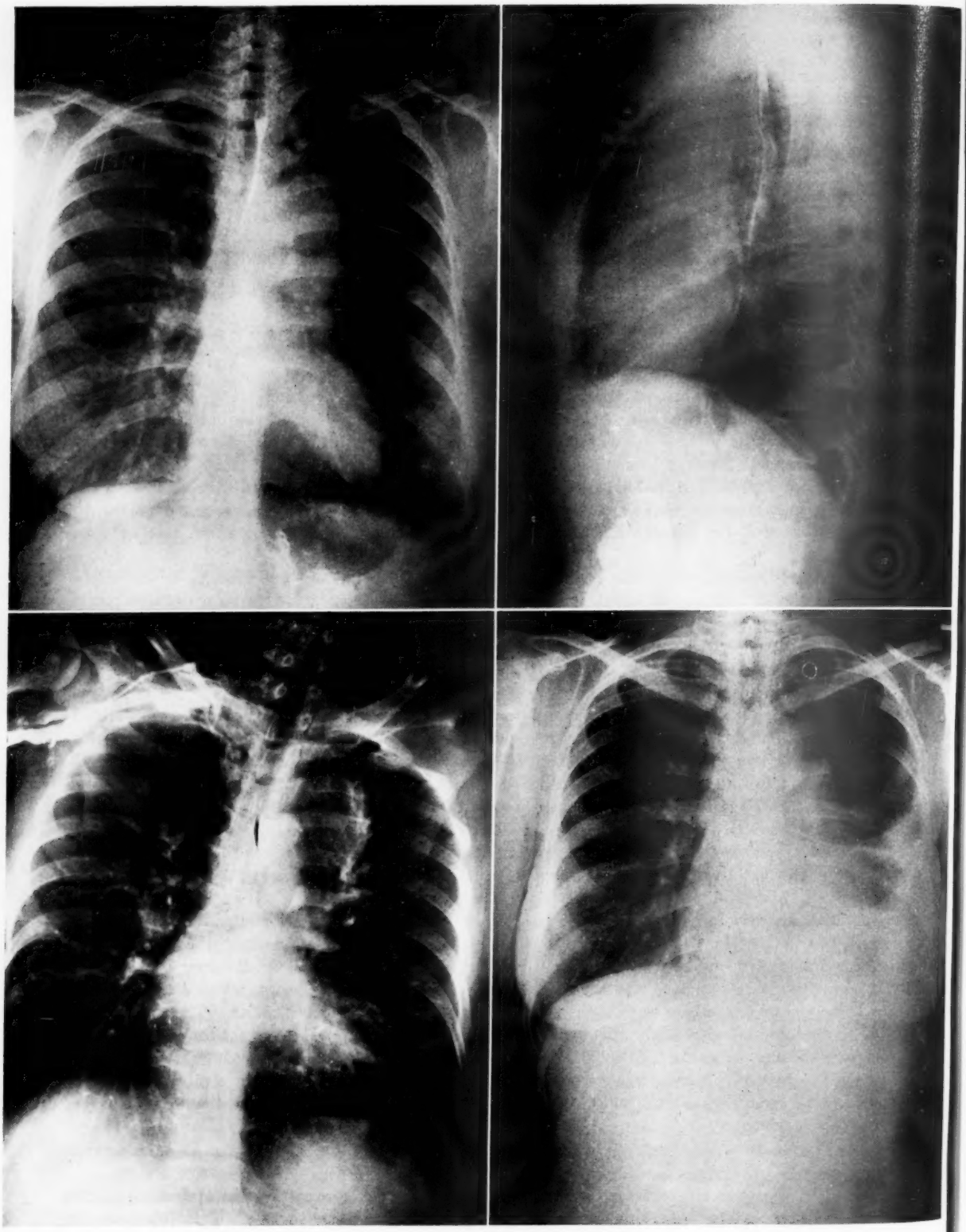

Fig. 3.

Fig. 4.

Fig. 1.—Posteroanterior roentgenogram of chest showing a left paramediastinal mass.

Fig. 2.—Left lateral roentgenogram of chest revealing the anterior location of the indistinctly demarcated density.

Fig. 3.—Angiocardiogram with dye in the left ventricle, aorta, and left common carotid artery. The tumor does not fill with Diodrast.

Fig. 4.—Posteroanterior roentgenogram of chest five weeks following last operation. The left lung is completely re-expanded and the sternum is held in good position by encircling wire sutures.

of streptokinase and 25,000 units of streptodornase were instilled in 10 c.c. dilutions in two separate locations in the left chest on Feb. 26, 1952. Thoracentesis the following day yielded 700 c.c. of thin, dark bloody fluid. No additional fluid could be obtained on repeated aspirations of the chest.

Because of increasing dyspnea and failure to control the clotted hemothorax by chemical decortication, the patient was returned to the operating room six days following the first operation.

Operation (Feb. 28, 1952).—With the patient supine, the anterior left chest was entered through the third intercostal space. The left pleural cavity contained numerous large fibrinous clots which were removed manually. A thin hemorrhagic membrane was seen covering the left lung partially immobilizing this structure. This was removed by alternate sharp and blunt dissection. Following the evacuation of the fibrinothorax and decortication of the thin membrane over the left lung, complete re-expansion of this structure was obtained with a small amount of positive pressure. The tumor which had been released partially from the heart and great vessels at the time of the previous operation was again seen to extend across the anterior superior mediastinum. A vertical incision was made over the mid-portion of the sternum extending from the episternal notch to the level of the sixth costal cartilage. The sternum was then split longitudinally in its mid-portion with a Lebsche sternal knife.

Fig. 5.—Photograph of gross specimen. Note thin-walled cystlike spaces which contained blood.

Following division of the internal mammary artery and vein between ligatures the incision in the sternum was extended across the left lateral margin of this structure so that it communicated with the incision in the third left intercostal space. The osteo-musculocutaneous flap was then retracted superiorly giving excellent exposure of the entire anterior mediastinum and great vessels. The tumor, which was quite large, and grossly similar to thymus, was seen to extend across the midline. It was intimately attached to the superior vena cava, left innominate vein, left carotid artery, left subclavian artery, arch of the aorta, and the upper portion of the left auricle and ventricle. The tumor appeared to be molded to the configuration of the structures just described and in one location sent fingerlike projections

around the left subclavian and carotid arteries so that these structures were of necessity completely mobilized at their point of origin from the arch of the aorta to obtain complete removal of the neoplasm. Before complete removal could be accomplished it was necessary to doubly ligate and divide a large vein 1 cm. in diameter which extended from the inferior aspect of the mid-portion of the left innominate vein to the upper pole of the tumor mass.

Fig. 6.—Photomicrograph of tumor. Blood-filled spaces are lined by a single layer of endothelium. No malignant changes are noted.

Following this extensive dissection the entire tumor was removed. The left chest was drained with intercostal catheters placed anteriorly and posteriorly and connected to water seal bottles. The sternum was reapproximated with encircling wire sutures and the thoracotomy incision was closed with interrupted sutures of No. 1 chromic catgut.

Following the second operation the patient made a rapid uneventful convalescence and was discharged home on her thirteenth postoperative day, at which time all incisions were completely healed and she was ambulatory without complaints.

Follow-up examination on April 5, 1952, approximately five weeks following the second operation, showed excellent re-expansion of the left lung and all wounds to be well healed. The patient complained of painful lactating breasts and was concerned about being pregnant. She had received several medical treatments in the past to make pregnancy possible. These had been unsuccessful. The patient was reassured that lactation was the result of the thoracic incisions after a careful examination revealed no other signs of pregnancy.[6]

Posteroanterior roentgenograms of the chest (Fig. 4) revealed some residual pleural density at the left base, but the lung was well expanded. The sternum remained in good approximation.

Pathology.—Grossly (Fig. 5), the tumor was a soft cystic mass measuring 12 by 7 cm. in diameter. Sections through the tumor showed the bulk of the mass to be made of thin-walled spaces, 1 to 5 mm. in diameter, which contained blood and were separated by tissue-paper thin, yellowish gray, fibrous septa. The entire mass was surrounded by a thin layer of fat tissue. A pseudo capsule was identified.

Microscopic examination of the specimen (Fig. 6) showed the tumor to be made up of large dilated blood-filled spaces separated by thin fibrous septa in which occasional smooth muscle bundles could be identified. The blood-filled spaces were lined by a thin layer of endothelium. The entire tumor mass was surrounded by fat tissue. There was no evidence of malignant degeneration.

Diagnosis.—The diagnosis was cavernous hemangioma.

SUMMARY

A rare mediastinal tumor of blood vascular origin (benign cavernous hemangioma) is reported. Complete surgical removal of the tumor was accomplished. Despite specialized investigations, including esophagoscopy, bronchoscopy, and angiocardiography, the case presented unusual problems in diagnosis and management because of the location of the tumor, its indistinct demarcation on roentgenograms of the chest, and false positive laboratory reports.

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INNOMINATE ARTERY ANEURYSM TREATED BY RESECTION AND END-TO-END ANASTOMOSIS

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ONLY fifty-one direct operative attempts to cure aneurysms of the innominate artery have been recorded.[1] Details concerning these attempts have been analyzed and summarized by Shumacker,[2] Gordon-Taylor,[3] and Lane and Peirce.[1] The operative mortality rate has been high (about 40 per cent) and the cure rate low. Proximal ligation has been the method most frequently employed, but it is now generally agreed that proximal and distal ligation, with excision of the sac when possible, offers the greatest likelihood of cure.

In operating recently upon a saccular aneurysm of the innominate artery, we found that circumstances were favorable for resection of the portion of the artery from which the aneurysm arose. Continuity was restored by end-to-end anastomosis of the divided ends of the innominate artery. This method of treatment has not been previously utilized, to our knowledge.

CASE REPORT

F. S., a 55-year-old white woman, was admitted to the Hospital of the University of Pennsylvania on May 16, 1950. She had noted intermittent pain in the right supraclavicular area for more than two years. For about three months prior to admission the pain was almost constant. During periods of physical exertion and emotional excitement she had difficulty in breathing, and she thought this was due to "pressure" in the right side of her neck. A serologic test for syphilis was found to be positive about a year before admission and she was given a course of penicillin and bismuth injections by her family physician at that time. Her family physician had also treated her for hypertension, which caused severe headaches, for several years.

Physical Examination.—The patient was moderately obese, weighing 190 pounds. She appeared well. The blood pressure was 200/110 in both arms. Temperature, pulse, and respiration were normal. At the base of the neck, behind and lateral to the right sternocleidomastoid muscle, there was a pulsatile mass which seemed somewhat larger on palpation than on inspection because of her obesity. A murmur was heard over the mass. There was no tracheal tug. The heart did not appear to be enlarged, but the aortic second sound was greatly accentuated. The rest of the examination was not remarkable.

Laboratory Studies.—A complete blood count and routine urinalysis were normal. The blood urea nitrogen, sugar CO_2, chloride, protein, and prothrombin levels were within normal limits. Blood Kolmer and Kline tests were positive.

X-ray Studies.—The heart did not appear enlarged and the lung fields were clear on a standard posterior-anterior chest film. The superior mediastinal shadow was wider than normal, especially on the right. There was deviation of the trachea to the left at the thoracic inlet.

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Angiocardiography revealed tortuosity of the right common carotid artery and an abnormal shadow just above the innominate artery (Fig. 1).

Preoperative Course.—While the above studies were in progress, the right common carotid artery was occluded by finger compression daily. The patient tolerated this procedure poorly. She usually complained so bitterly of pain after two to three minutes of compression that an adequate test of carotid occlusion was not possible. On one occasion she permitted carotid compression for ten minutes and there was no evidence of cerebral ischemia during this period.

Operation.—Operation was performed on the sixth day after admission. An incision was made along the anterior border of the right sternocleidomastoid muscle, under local anesthesia, with the patient in the supine position. The right common carotid artery was mobilized and occluded at its mid-portion with a Crafoord aortic clamp for forty minutes. During this period the sensorium was clear, the vital signs did not change, and there was no weakness of the muscles on the left side of the body. This was regarded as evidence that carotid occlusion would probably be tolerated during the insertion of a vein graft or any other procedure which might be necessary for restoration of blood flow following resection of the aneurysm.

Fig. 1.—Preoperative angiocardiogram. The aneurysm can be seen just above the innominate artery. The trachea is displaced to the left by the aneurysm. The right common carotid artery is very tortuous.

General anesthesia was then administered and an endotracheal tube was inserted. The method of exposure recommended by Shumacker[4] was employed (Fig. 2). The lower end of the cervical incision was extended downward over the sternum to the level of the third interspace. The sternum was divided beneath the skin incision and transected at the level of the third interspace. A portion of the medial third of the right clavicle was resected and the left clavicle was divided at the junction of the inner and middle thirds. A rib spreader was inserted and the exposure illustrated in Fig. 3 was obtained. It was found that the aneurysm arose from the posterosuperior aspect of the mid-portion of the innominate artery and extended upward along the right side of the trachea, which was displaced to the left. An endoaneurysmorrhaphy was not possible because of the location of the neck of the sac. One Crafoord aortic clamp was placed across the base of the innominate artery and another just proximal

to its bifurcation. A 2.5 cm. segment of the innominate artery, which included the neck of the aneurysm, was excised. All of the aneurysmal sac was removed except for an area about 2 cm. in diameter which was adherent to the trachea. The divided ends of the innominate artery were brought together without difficulty. The walls of the artery were greatly thickened and contained many calcified plaques, presumably as the result of both syphilitic and arteriosclerotic involvement. Suturing was begun with 00000 Deknatel silk on an atraumatic needle. It soon became apparent, however, that a needle of this size was unsatisfactory. The needle either broke when calcified material was encountered, or was not long enough to pass through the wall. Curved intestinal needles, threaded with 000 silk, were then used. These needles proved to be adequate, but suturing was still difficult and time consuming. Interrupted sutures were used throughout and when the anastomosis was completed, the innominate artery had been occluded for fifty-seven minutes. Two or three additional sutures were required to obtain a blood-tight closure. The edges of the sternum were approximated with heavy wire sutures and the soft tissues were closed in the usual way. Drainage was not used.

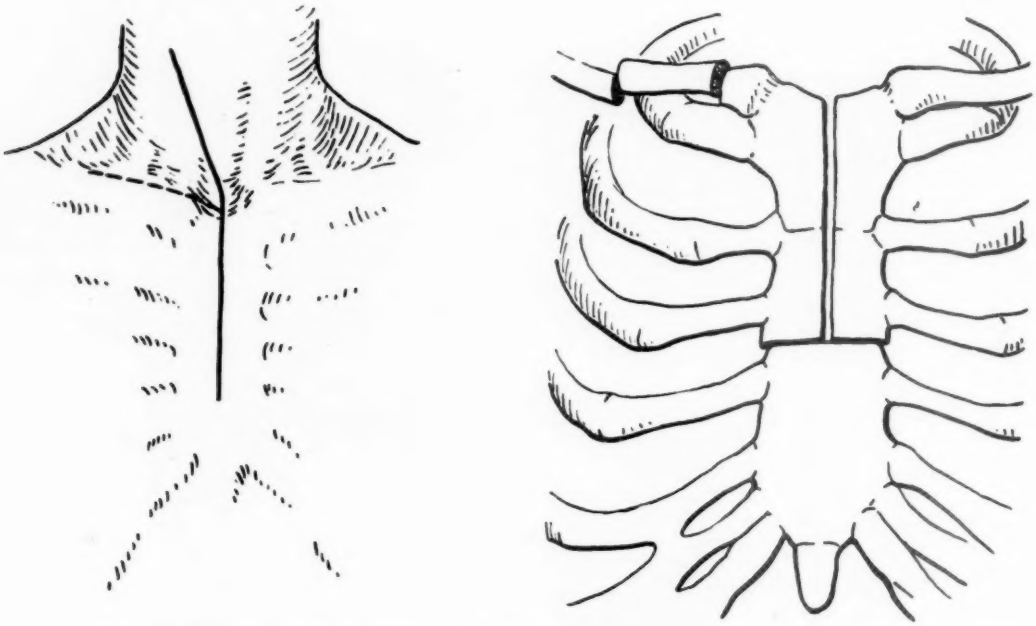

Fig. 2.—This drawing illustrates the method of achieving the type of exposure obtained. The skin incision is shown on the left. The dotted line represents an alternative incision which may be used when exposure high in the neck is not needed. Division of the sternum to the level of the third interspace and transection at that point are shown on the right. A portion of the medial third of the right clavicle is resected. In the instance described, the left clavicle was also divided.

Postoperative Course.—During the first twenty-four hours after operation the patient was unconscious and did not move her left arm or leg. During the next three or four days she gradually regained control of her mental facilities and of the use of her left leg. Her left arm remained paralyzed, however, except for slight motion of the shoulder girdle. The wound healed per primam. She was discharged on the seventeenth postoperative day.

The patient has been relieved of tracheal compression and of pain in the right supraclavicular area. When she was last seen, nearly two years after operation, it was estimated that she had 50 per cent disability of her left shoulder and elbow and 75 per cent disability of her left hand. Hypertensive headaches had increased in frequency. There were strong pulsations of the right common carotid artery.

DISCUSSION

The absence of untoward signs and symptoms during occlusion of the right common carotid artery under local anesthesia for forty minutes did not prove to be reliable evidence that the patient could withstand innominate artery occlusion for fifty-seven minutes. It seems likely that this was because of deprivation of blood flow through the right vertebral artery with innominate, but not with carotid, occlusion. The test of occlusion might have been reliable if it had included clamping of the right subclavian artery at its origin. An additional speculation is that the period of carotid occlusion might have decreased the patient's tolerance to innominate occlusion.

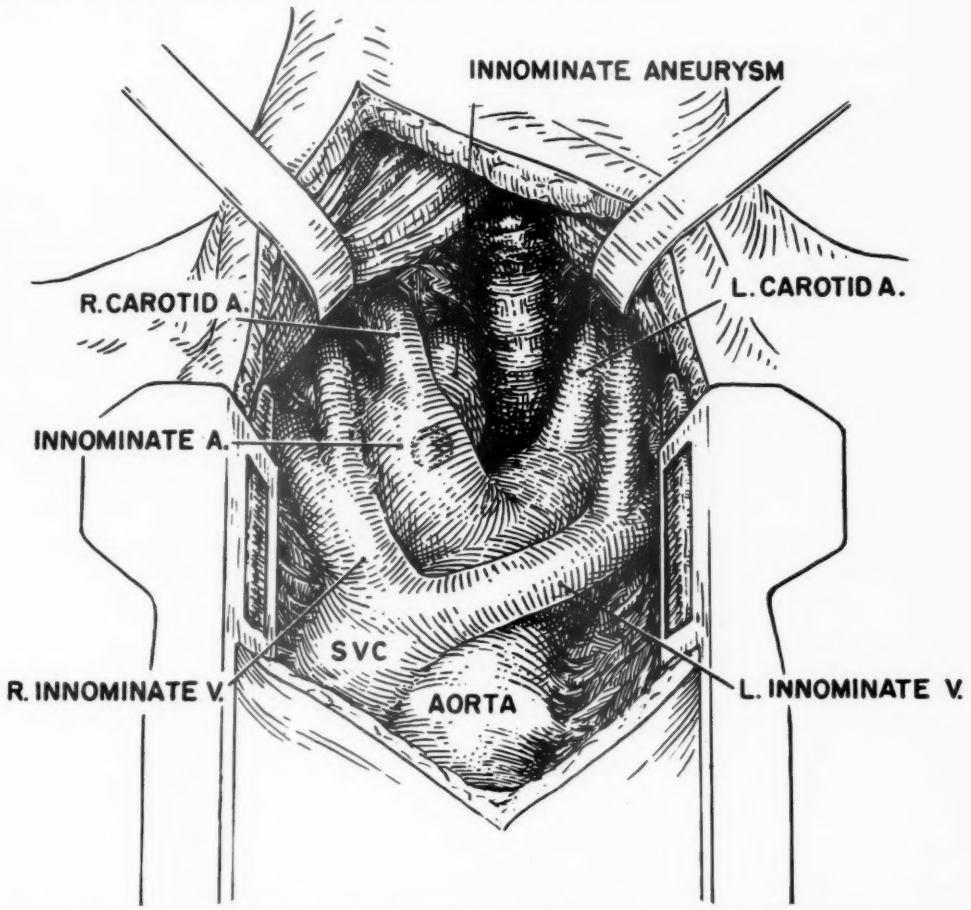

Fig. 3.—The exposure obtained, the relations of the great vessels, and the location of the aneurysm are illustrated diagrammatically.

The degenerative changes in the walls of this patient's innominate artery were so severe that the feasibility of suture was open to question. We were gratified to learn that an end-to-end anastomosis can be successfully performed under such circumstances. Valuable time was lost in attempting to use the usual 00000 arterial silk on delicate atraumatic needles. We believe it is important to recognize that heavier needles and silk are necessary when there is such extensive thickening and calcification of the arterial walls.

SUMMARY

An instance of successful resection of a segment of the innominate artery which included the neck of a saccular aneurysm has been reported. Continuity was restored by end-to-end anastomosis of the divided ends of the innominate artery.

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CARCINOID TUMORS OF THE RECTUM

A Report of Three Cases

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CARCINOID tumors of the gastrointestinal tract have been recognized throughout the twentieth century but few carcinoids of the rectum have been reported until the last decade. The first of these cases to appear in American literature was that reported by Brunschwig in 1933.[3] As late as 1942 Stout[20] found only 6 such cases reported in the world literature and added 6 more to that number. Horn[9] in 1949 was able to find 50 cases and add 6 more which he had seen. Since then 24 have been mentioned in the American literature (Mayo and McKee 2, Shepherd 2, Hines 3, Rosser 1, Wilson 1, Pearson and Fitzgerald 7, Raven 1, and Tavenner 7[11, 12, 16, 18, 19, 23]), making a total of 80 cases reported. This sudden increase in the number of cases reported apparently indicates an improved knowledge of the subject by the clinician and pathologist. Undoubtedly many more have been diagnosed and not reported, and others have been seen and misdiagnosed.

Carcinoid tumors have been reported in almost all portions of the gastrointestinal tract. Ashworth and Wallace[2] in 1941 reported 25 carcinoids in "unusual locations" (i.e., other than the ileocecal region). To this number they added a case of carcinoid of a Meckel's diverticulum. Pearson and Fitzgerald[13] in 1949 listed carcinoids of the stomach, duodenum, gall bladder, jejunum, cecum, colon, rectum, and Meckel's diverticulum. The 3 most common sites are the appendix, terminal ileum, and rectum, in that order.[5, 14, 15, 22]

It is the generally accepted opinion of most writers that these tumors arise from the cells of Kultschitzky found in the crypts of Lieberkühn. These cells have been thoroughly investigated from time to time since the beginning of the twentieth century and, therefore, have had many names attached to them. The most common of these names are listed by Stout as yellow cells, chromaffin cells, basigranular cells, cells of Nicolas, Kultschitzky, Schmidt and Ciaccio. He referred to these cells in the rectum as Erspamer's pre-enterochrome cells. The cells are found throughout the gastrointestinal tract and according to Maximow and Bloom are more common in the appendix than in the small intestine. They are believed to grow out of the bottom of the glands in the connective tissue of its lamina propria. They may be scattered singly or may be seen in groups in the mucosal wall. Usually there are about 5 to 10 in each crypt of Lieberkühm lying scattered among the mucous secreting cells of the crypts. They are usually pyramidal or wedge-shaped cells with the base rest-

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ing upon the basement membranes and the apices usually not reaching as far as the lumen of the crypts. They have nuclei elevated above the basaly situated nuclei of the neighboring cells and in the basilar portion of the cytoplasm are found a considerable number of fine granules.

There has been much speculation as to the etiology of these cells. Raiford[15] feels that these cells are of ectodermal origin which have migrated early in life from the neural crest and have become adapted to the special function of forming a part of the general chromaffin system. The argument in favor of this origin is the striking similarity of the cells of some of these tumors to the cells of adrenal gland. Others, such as Porter and Whelan,[14] have suggested that they came from endodermal origin. The cells have an affinity for silver stains and therefore have been termed the argentaffin cells. Porter and Whelan have reported recently that these cells have a definite affinity for lead, which can be seen with hematoxin. The only other cells which have been noted to show plubiphilic granules, similar to those in argentaffin tumors, are those of the adrenal medulla.

Some excellent reviews of the pathologic appearance of carcinoid tumors have been written by Stout,[20] and Pearson and Fitzgerald.[12, 13] The tumors are usually composed of uniform cells of small to moderate size, growing in cords and ribbons; Stout, however, points out that carcinoids of the rectum do not necessarily follow this pattern, but instead may have solid masses of polygonal cells or "carelessly coiled" ribbonlike festoons of columnar and prismatic cells, as was noted in several of his cases. There may be other cell patterns that are less outstanding, such as the polygonal cells, interwoven in these festoons. It was once thought that a tumor could not be diagnosed as carcinoid unless it took a silver stain; however, most pathologists now agree that the histologic structure itself is sufficiently distinctive to permit diagnosis. This is especially true in the rectum where very few of the cases have taken these stains. Stout explains this by reasoning that rectal carcinoids originate in Espamer's preenterochrome cells, in which the enzyme enteramin, necessary to reduce silver, is absent.

The marked similarity of these tumors on microscopic examination to basal cell carcinomas, to the islet cells of the pancreas, and to bronchial adenomata (carcinoid type), has been noted. Their varying appearance has produced a multiplicity of names, of which, of course, the most common is carcinoid. They have also been called mucous membrane nevi, immature sympathetic neurocytomas, argentaffinomas, small-cell carcinomas, and neurocrine tumors. Whether the name carcinoid is sufficient has been questioned many times. Oberndorfer, in 1907, used this term originally because he believed them to be benign, but similar in appearance to carcinoma. The name is so well fixed in the literature that it seems only logical to continue with it and hope that all clinicians will realize that these tumors are all potentially malignant whether found in the appendix, ileum, or rectum.

CASE REPORTS

CASE 1.—P. G. D., a 34-year-old white sailor, was admitted to the United States Naval Hospital, Portsmouth, Va., on April 11, 1950, with a diagnosis of malignant pelvic tumor,

type undetermined. His illness dated from November, 1949, when he had had low-back pain and indigestion. He was treated at that time by a civilian doctor for kidney trouble with partial relief, there being a residual constant low-back pain. During the three months preceding admission, he noticed a moderate weight loss, moderate constipation and irregularity in the time of bowel movements, and occasional nocturia. The past history and family history were noncontributory.

On March 24, 1950, the patient had acute urinary retention without any signs of urinary infection. He was admitted to a hospital ship where he further developed symptoms of intestinal obstruction. At operation aboard the hospital ship a large, fixed tumor mass which entirely filled the pelvis was found. This mass was adherent to the colon and to the bladder and was very highly vascular. The surgeon describes the mass as having a caput medusae of blood vessels. A biopsy was obtained at that time and a frozen section reported as carcinoma. The case was then considered inoperable, the abdomen was closed, and the patient was transferred to this hospital on April 11, 1950.

On arrival he showed evidence of some weight loss and a moderate secondary anemia. He showed no clinical evidence of metastasis or of impaired renal function. The abdominal wound was well healed. The admission white blood count was 4,700, the red blood count was 4,300,000 with 12 Gm. of hemoglobin. The urinalysis showed 100 mg. of albumin and 8 to 10 white blood cells per high powered field. The blood Kahn was reported as negative; preoperative blood chemistry was all within normal limits. A barium enema revealed an obstructing lesion at about 6 cm. The barium was passed by this portion of the colon with great difficulty and no intrinsic bowel defect could be found. The colon was markedly displaced by the large mass lying within the pelvis. A retrograde pyelogram showed both kidneys and ureters to be normal except that the right ureter was tortuous and appeared to lie somewhat anterior to its usual position in the lower portion. The bladder was well shown in one of the films (Fig. 1). It was large, slightly less dense on the left than on the right, suggesting decreased filling due to compression by the adjacent mass on the left. The entire bladder was markedly displaced toward the right. No definite osseous abnormality was observed. The impression was that of a large pelvic mass containing calcium, appearing to be well circumscribed on the left margin, causing displacement of the bladder and partial obstruction of the colon. The mass was believed to be extravesicular. The patient was presented to the Tumor Board on April 25, 1950. At that time a review of the biopsy slides taken during the exploratory laparotomy aboard the hospital ship revealed a difference of opinion. It was felt, however, that this could be a carcinoid and that surgical exploration was indicated.

On May 8, 1950, a celiotomy was performed through a left rectus incision extending from the symphysis to a point above the umbilicus. A large, rounded, circumscribed mass involving the entire pelvic cavity was found. No regional lymph nodes were palpable. The liver was normal. Other findings were essentially normal. The rectum was obstructed and the entire colon filled with inspissated fecal material. The peritoneum was reflected upward and by blunt dissection the tumor was freed from its attachments superiorly and posteriorly. The dissection was performed with some difficulty due to the size of the tumor. It was finally delivered; the pedicles remaining on the right lateral portion were ligated. Several large vessels deep in the pelvis could not be ligated and the wound was closed around the hemostatic clamps, which were removed at a later date. Considerable hemorrhage was encountered throughout the entire procedure. The patient received 3,500 c.c. of blood in order to maintain his blood pressure and to cover an estimated loss of approximately 4,000 c.c. during the operation. After a stormy course in the immediate postoperative period the patient progressed normally and gained weight rapidly. Microscopic sections of the tumor showed a typical carcinoid with areas of degeneration (Fig. 2).

On Aug. 1, 1950, a sigmoidoscopic examination was given and a rectal polyp was removed at about 6 cm. on the anterior wall, almost at the site where the previous pelvic carcinoid had been attached. This polyp was reported as a carcinoid of the rectum. Another rectal polyp was removed on Aug. 20, 1950, and was reported as inflammatory. Post-

operative barium enema and retrograde pyelograms revealed a normal genitourinary tract and a normal colon. The patient was discharged to duty on Sept. 20, 1950. He was readmitted to this hospital in June, 1951, and April, 1952, for follow-up purposes. At these times cystoscopic and sigmoidoscopic examinations were entirely normal, as were barium enemas and retrograde pyelograms. There was no evidence of any recurrence of the carcinoid and no evidence of distant metastasis.

Fig. 1 (Case 1).—Roentgenogram showing the marked displacement of the bladder by the metastatic pelvic lesion.

CASE 2.—D. B., a 33-year-old Aviation Machinist Mate in the United States Navy, was admitted to the United States Naval Hospital, Portsmouth, Va., on Aug. 10, 1951, with diagnosis undetermined (rectosigmoid tumor). The patient was in good health until 5 to 6 weeks before admission when he began to have 3 to 4 soft bowel movements daily, with blood and small pieces of tissue intermittently mixed with the stool. He had been seen by a physician in June of 1951 and was given some ointment for treatment of this condition without relief. Aboard ship he was seen and sigmoidoscoped and a rectosigmoid lesion was found. The patient was then transferred to this hospital. He had gained two pounds from the onset of his illness until admission and had had very slight intermittent diffuse abdominal pains during his preadmission course. The system review was entirely negative

except for pain noted in the lower abdomen while doing some heavy work, eighteen months before the onset of his present illness. Past medical history was noncontributory.

Physical examination was entirely normal except for a firm, fixed mass on the posterior wall of the rectum at the tip of the examining finger, involving one-half of the circumference of the bowel. Laboratory studies including hemoglobin, white cell count, urinalysis, and serology were all within normal limits. His barium enema revealed a constant filling defect, measuring approximately 2 cm. in diameter, at the junction of the sigmoid and the rectal ampulla on the anterior wall of the colon (Fig. 3). Sigmoidoscopic examination showed a fungating, ulcerating, firm 5 cm. lesion, at 10 cm. on the anterior wall; this appeared to be a typical adenocarcinoma of the rectum (Fig. 4). Biopsy of the lesion with biopsy forceps was performed and the report was malignant neoplasm in the rectum, site of origin undetermined. Repeat biopsy produced the same indefinite diagnosis.

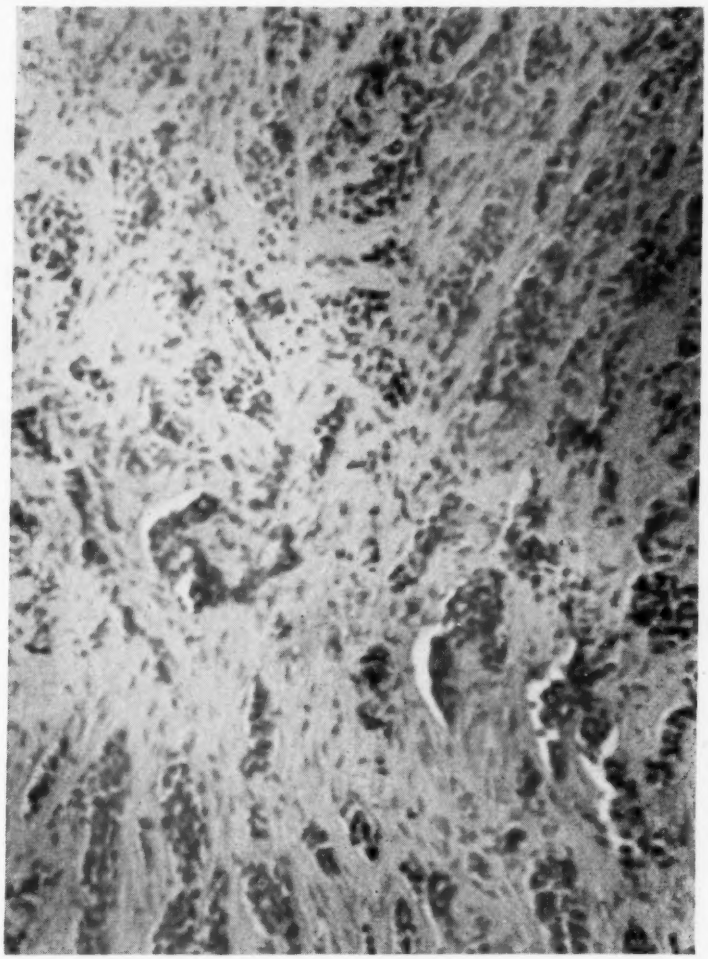

Fig. 2 (Case 1).—High-powered magnification showing sheets of carcinoid cells.

Because of the appearance of the tumor it was felt that it was an adenocarcinoma of the rectum; the patient was prepared preoperatively with oral terramycin, and operation was performed on Aug. 23, 1951. The abdomen was opened through a lower mid-line incision; in the rectosigmoid colon just above the peritoneal reflection there was a large grayish tumor mass which had broken through to involve the peritoneum just above the lesion. A careful examination of the mesocolon, periaortic nodes, and the liver failed to

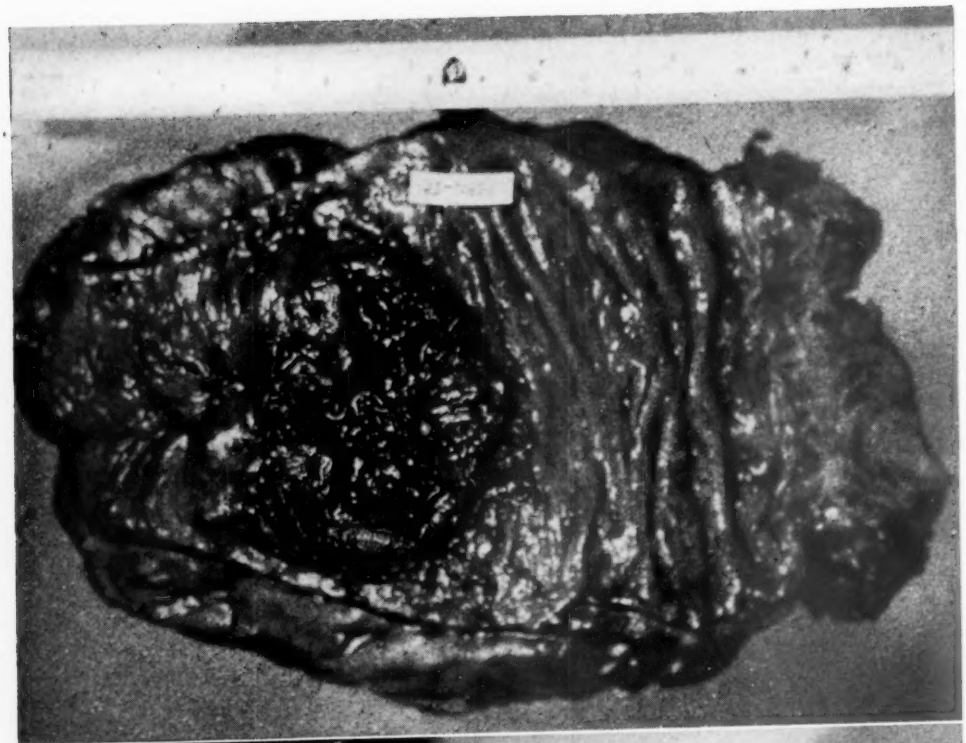

Fig. 4.

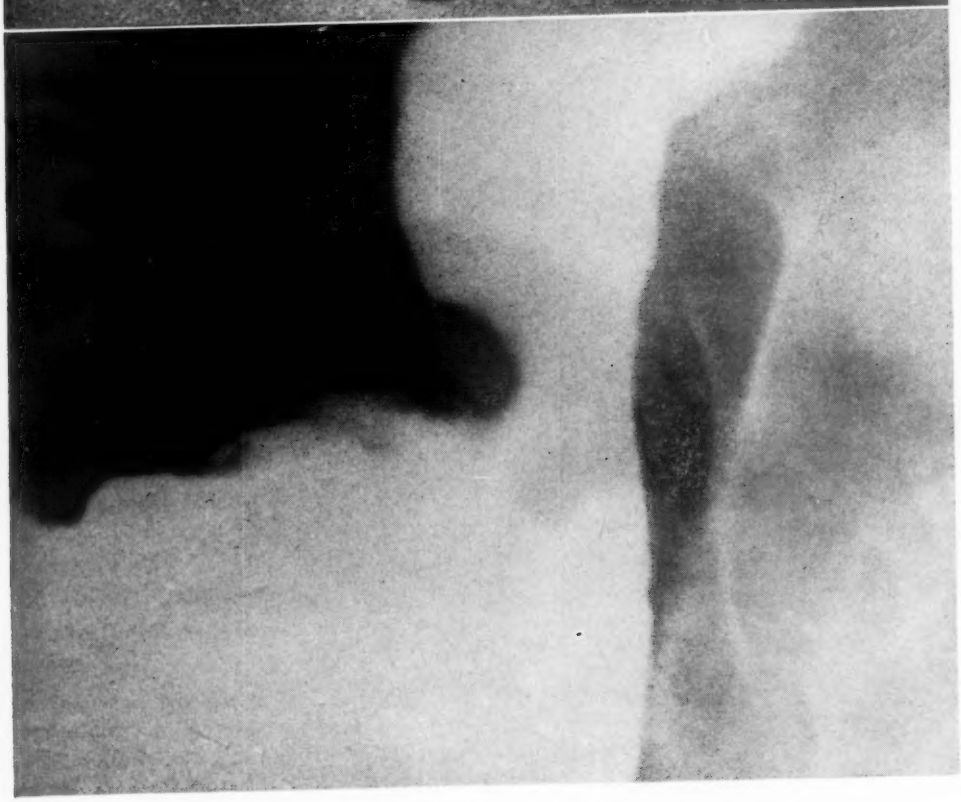

Fig. 3.

Fig. 3 (Case 2).—Barium enema showing filling defect at rectosigmoid junction.
Fig. 4 (Case 2).—Gross specimen following abdominoperineal resection. The appearance is that of adenocarcinoma.

reveal any other metastatic lesions. Because the appearance of the lesion was that of an adenocarcinoma of the rectum and because the lesion had broken through the bowel wall to involve the peritoneum, a combined abdominal perineal resection was performed.

The postoperative course was uncomplicated. The patient was able to void spontaneously and on the third postoperative day the colostomy clamp was removed and the colostomy stoma began to function. The posterior pack was removed on the fifth postoperative day. On Dec. 4, 1951, the posterior wound had healed and the colostomy was functioning well. There was no evidence of any metastasis and the patient was discharged from the service in March, 1952. The pathologic report showed a typical carcinoid tumor with invasion of the entire bowel wall (Fig. 5). The regional nodes were not involved.

CASE 3.—D. L., a 20-year-old white man, was admitted to the United States Naval Hospital, Portsmouth, Va., on Jan. 31, 1952, with a history of intermittent bleeding, during and following bowel movements, for three weeks prior to admission. He had noted some tendency toward constipation during this period, but it was not severe and there was no tenesmus. There was no history of pain with bowel movements, no loss of weight, and no known tarry stools.

On admission physical findings were entirely within normal limits except for the rectal examination. A firm, rubbery, 1 cm. diameter polyp 6 cm. from the anus on the anterior wall was seen, and removed with biopsy forceps. No other anorectal pathology was noted.

The microscopic sections showed this to be a carcinoid (Fig. 6); accordingly six days later excision of the previously biopsied area was carried out, taking 0.5 to 1 cm. of normal mucosa on all sides of the original biopsy scar and excising down to the muscularis in the vertical plane. This was carried out with a scalpel, and the resulting wound was closed. No tumor cells were found in the second area of resection.

The patient's rectal bleeding ceased after the initial removal of the rectal tumor and did not recur during his hospital course.

The condition was explained to the patient, and he was discharged to duty on Feb. 19, 1952, with recommendation for follow-up sigmoidoscopic examination every three months.

CLINICAL PICTURE

There are, including these 3 cases, 41 reported carcinoids of the rectum about which we can gather sufficient information to get an idea of the symptomatology and appearance of the lesion.

The symptoms seen in cases of carcinoid depend on its location in the gastrointestinal tract. In the appendix it may give obstructive symptoms and mimic, or be productive of, acute appendicitis. Those seen in the ileum may give signs of incomplete intestinal obstruction late in their course due to partial filling of the lumen. In this series of 83 cases of carcinoid of the rectum, 42 cases have no symptomatology reported, either no clinical history was noted, or the tumor was an incidental autopsy finding. Of the remaining 41 cases, 17 were discovered on routine rectal examination and 24 had a chief complaint referable to the anorectal area; 15 of these latter had rectal bleeding. It is difficult to evaluate this symptom in the majority of these cases, however, because they also present hemorrhoids, fissures, fistulas, or some other rectal condition which could have produced the bleeding. Some few cases, such as that reported by Yaker, presented signs of obstructive sensation on defecation. To a large extent, however, these tumors remain symptomless, or present symptoms which are overshadowed in the face of adjacent and associated pathology, and discovery occurs only during routine rectal and proctosigmoidoscopic examination.

Fig. 5.

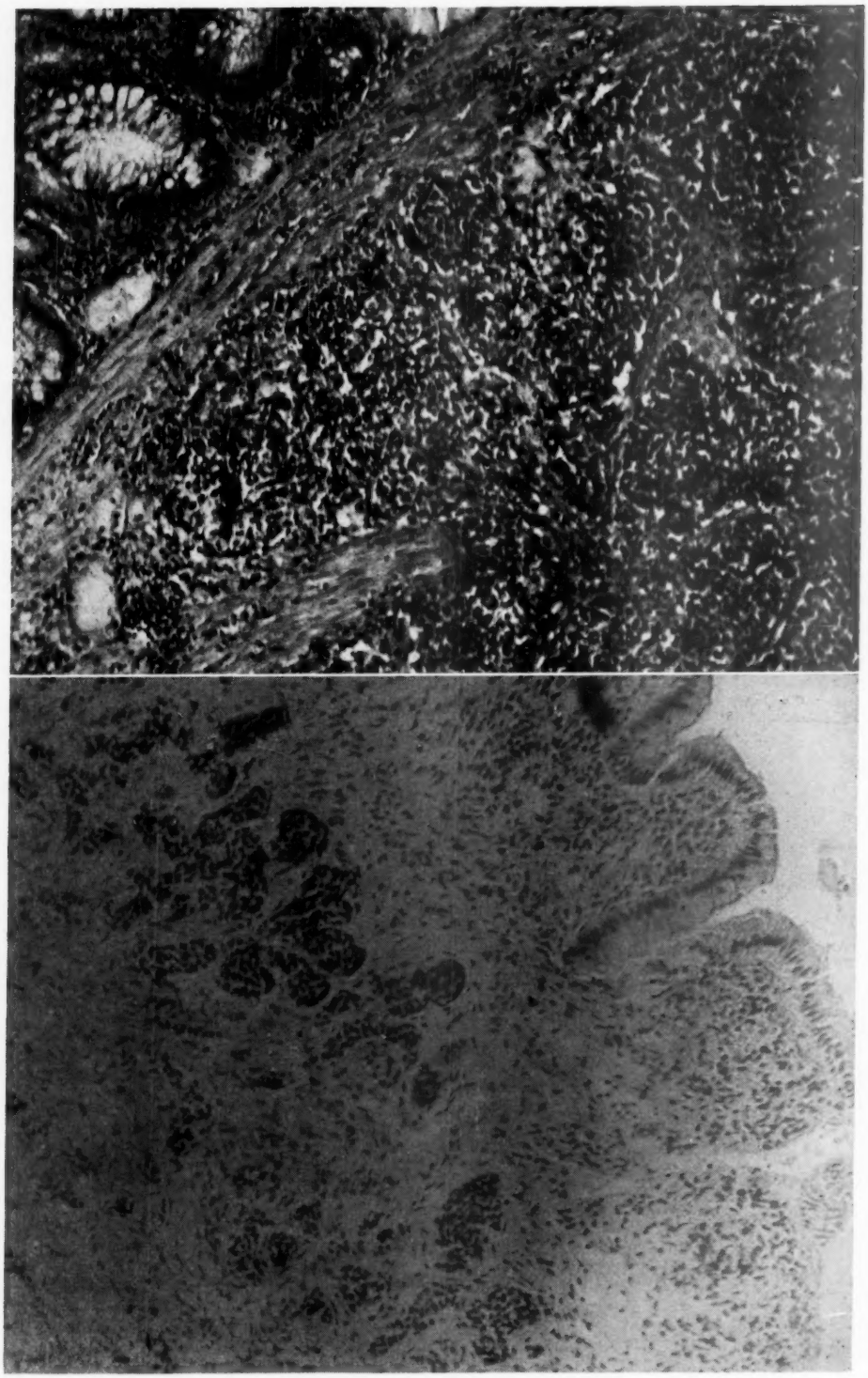

Fig. 6.

Fig. 5 (Case 2).—Low-power magnification showing carcinoid cells beneath normal mucosa.
Fig. 6 (Case 3).—Low-power magnification showing carcinoid cells beneath mucosa in a rectal polyp.

Carcinoids of the rectum, like carcinoids found in other regions, are usually single submucosal nodules. The majority are sessile polyps, but pedunculated polyps and plaques are also seen. Most cases recorded have been freely movable, but there are cases reported, such as that of D. B. (Case 2), which have had infiltration of the muscularis and serosa. To our knowledge there are only 6 cases (or 7.5 per cent of the entire series) which have had a primary tumor larger than 3 cm. in diameter. On the other hand, as will be pointed out below, 12 per cent of these tumors have metastasized. It is obvious that the presence of a small polypoid primary lesion, therefore, does not rule out the possibility of metastasis in this disease any more than in any other malignancy. It is often impossible to distinguish grossly between carcinoid and benign rectal masses, such as adenomatous polyps, and, therefore, excision biopsy of all small rectal tumors is extremely important. In Jackman's series of 87 submucosal rectal nodules[10] he found 4 carcinoids, none of which were able to be diffierentiated grossly from simple polyps, fibromas, lymphomas, or similar growths. Microscopic diagnosis is the only diagnosis of this disease.

AGE AND SEX INCIDENCE

The age of the patients with carcinoid of the rectum varies from 14 to 71 years. Of the patients of whom we know the age the average is 44 years; the average age of the men in this group is 46 years and of women 43 years. This is higher than that given for carcinoid of the appendix, which is listed by Grimes and Bell[6] as 29.5 years, and by Pearson and Fitzgerald[13] as 25 years. However, it is much lower than the age of patients seen with carcinoid of the small intestine. Grimes and Bell[6] gave the figure as 58 years for the average age of this group; Pearson and Fitzgerald, 67 years of age.[13] In those cases of carcinoid of the rectum in which the sex is known, there have been about 3 women to every 2 men. Carcinoids of the appendix have been reported in a ratio of 5 men to each 3 women; in the small intestine they are seen more commonly in women. Carcinoids of the rectum are recorded in both Negro and white, Hebrew and Gentile. Thus far, there seems no predilection for any one group.

MALIGNANCY

Carcinoids are found in may places in the gastrointestinal tract; they are most commonly noted in the appendix (0.2 to 0.5 per cent of all surgically removed appendices have contained carcinoid[14]). Appendiceal carcinoids very rarely metastasize. Porter and Whelan reported 72 carcinoids, with no metastases, in a series of 26,384 surgically removed appendices.[14] Up to 1946 only 22 malignant appendiceal carcinoids were reported.[1]

The tumor next most frequently occurs in the terminal ileum (although only about one-tenth as frequently as in the appendix) and then with decreasing frequency in the rectum, jejunum, colon, cecum, stomach, gall bladder, and duodenum. Carcinoids in Meckel's diverticuli and dermoid cysts of the ovary have been reported. All of these extra-appendiceal carcinoids are clinically much more malignant; Pearson and Fitzgerald reported 38 per cent metastases

in this group,[13] and other authors emphasize the malignant nature of these extra-appendiceal tumors.[2, 6, 22]

Including the 2 malignant carcinoids reported here, there are now 10 known cases of metastatic carcinoid of the rectum; this represents 12 per cent of the entire group. We believe this percentage of clinical malignancy is significantly smaller than that reported for the small bowel carcinoids, and this difference may be due to earlier discovery via routine proctosigmoidoscopy. (Possibly there is a difference in carcinoid cell structure in this location, as shown by the failure of many rectal carcinoids to take a silver stain; if so, the nature of the difference is not known.)

We believe that a rational explanation for the clinical behavior of the variously located carcinoids, however, may be found by a tabulation such as that set forth in Table I. It seems possible that carcinoids in all locations are similar in their growth and malignancy patterns, but those that are discovered earlier clinically, because they are so situated as to produce early symptoms or to be visible in thorough routine examinations, are removed before metastases have time to develop.

TABLE I. RELATIONSHIP OF LOCATION, AGE, AND REPORTED MALIGNANCY

LOCATION	AVERAGE AGE	METASTASIS
Appendix	25 to 29	Very uncommon (22 known cases)
Rectum	44	12 per cent
Small intestine	58 to 67	About 38 per cent

TREATMENT

There have been 29 reported carcinoids of the rectum in which the tumor has been excised locally. In this group, the follow-up varies from none to nine years,[4] with no known recurrences to date. Seven patients, including one of ours, have had abdominoperineal resections.[18, 19, 21, 23] In almost all of these cases the original microscopic diagnosis was carcinoma. Shepherd's 2 cases were reported as aniplastic carcinoma. One of Rosser's was reported as invasive carcinoma. Tavenner's case was reported initially as small-cell scirrhous carcinoma. The follow-up on all of these cases has been too short to evaluate the result of abdominoperineal resection in locally invasive carcinoids; however, it appears from the behavior of carcinoids located elsewhere in the gastrointestinal tract that the ten-year cure rate will be high.

Raven in his article[16] put forth a plan for the treatment of rectal carcinoids to which we concur; namely: "When a carcinoid tumour has been excised in the belief that it was an adenomatous polyp, subsequent histological examination proving the diagnosis, the patient should be kept under observation in order to detect any recurrence. When a small, non-infiltrating carcinoid is found and confirmed by biopsy, a wide, local incision is performed and the patient kept under observation. A radical operation is performed when a large carcinoid with infiltrating properties, or an annular constricting carcinoid, is present. If a recurrent carcinoid appears, a radical operation should

be carried out." To this we would like to add: Solitary distant metastatic lesions should be excised.

The use of x-ray and radium in the treatment of these tumors has been infrequent and no conclusions can be drawn. Grimes and Bell used x-ray treatments in two cases with questionable value.[6] Rosser used radium seed implants in metastatic lesions and seemed to get favorable and local result, but the patient died shortly thereafter of other generalized metasases,[18] and Yaker,[24] after local excision of a carcinoid 4 inches from the anus, treated the area with radium needles. There was no recurrence after eighteen months. However, there are many cases reported in which there has been no recurrence over the same period of time with local excision alone. It seems doubtful that x-ray or radium has much to offer in the treatment of this tumor.

SUMMARY

1. A discussion of the pathology of carcinoid tumors of the rectum, with a review of the literature, is presented.

2. Three cases of carcinoid of the rectum are described; 2 of these lesions were clinically malignant.

3. The malignancy and clinical characteristics of these lesions are discussed.

4. The characteristics of carcinoid tumors vary according to their location in the gastrointestinal tract; an explanation for this variance is offered.

5. It is emphasized that metastasis can occur from small rectal carcinoids.

6. A therapeutic approach to rectal carcinoids is outlined.

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Surgical History

CONDUCTED BY JOHN R. PAINE, M.D.

THE IMPACT OF RÖNTGEN'S DISCOVERY UPON THE TREATMENT OF FRACTURES

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PERHAPS no better example could be chosen to illustrate the dependence of progress in medicine upon progress in the basic sciences than to recall the effect of the discovery of x-rays upon the treatment of fractures. An adequate technology was already in existence; anesthesia, antisepsis, techniques of manipulation and internal fixation, and an appreciation of the pathologic anatomy of fractures. The treatment of fractures was handicapped by lack of means by which to make an accurate appraisal of the fracture before, during, and after treatment. Röntgen's discovery provided the means. The speed with which the x-rays were exploited in treating fractures testifies to the pressing need for a better method of diagnosis.

THE DISCOVERY

Professor Röntgen, at this time Director of the Physical Institute of the University of Würzburg, on a Friday evening, Nov. 8, 1895, was repeating the experiments of Hertz and Lenard on cathode rays. Suddenly in the darkened room he noted a bright fluorescence of some crystals lying upon the table some distance away from the tube. His interest aroused by this phenomena. Röntgen carried out an intensive investigation, the results of which were embodied in a brief paper, "On a New Kind of Rays," which was submitted for publication on Dec. 28, 1895. This report, mentioning the first photograph of the bones of a living hand, was published in the *Annals of the Physical Medical Society of Wurzburg* during the first week of 1896.[11] Its publication set off a chain of events which has affected all mankind, and, for its author, culminated in the award of the first Nobel Prize in physics in 1901. Public reaction to the discovery was instantaneous, and its practical applications in medicine were immediately recognized by doctors and laymen alike. The *Frankfurter Zeitung* for Tuesday, Jan. 7, 1896, carried the following note:[11]

> At the present time, we wish only to call attention to importance this discovery would have in the diagnosis of disease and injuries of the bones, if the process can be developed technically so that not only the humann hand can be photographed, but the details of other bones may be shown without the flesh.

*Markle Scholar in Medical Science.

> The surgeon then could determine the extent of a complicated bone fracture without the manual examination which is so painful to the patient; he could find the position of a foreign body, such as a bullet or piece of shell, much more easily than has been possible heretofore and without any painful examinations with a probe. Such photographs also would be extremely valuable in diagnosing bone diseases which do not originate from an injury and would help to guide the way in therapy.

The dissemination of information about the "new rays" proceeded with such speed that when a translation of Röntgen's article appeared in *Science*, Feb. 14, 1896, it was accompanied by notes and reproductions of x-ray photographs made by M. I. Pupin of Columbia College, Edwin B. Frost of Dartmouth College, and Arthur W. Goodspeed of the University of Pennsylvania.[23] In 1896 alone, 1,044 scientific books and articles dealing with the discovery were published in the world literature, as well as countless newspaper and magazine articles directed at the public.[11] How did this come about?

Röntgen's original publication was a model of scientific exposition. It contained a complete description of the equipment and methods employed. It was rapidly translated into many languages and was published in scientific journals throughout the world. The equipment needed to reproduce his experiment was readily available in every physical laboratory. As a result, any investigator could demonstrate the action of x-rays by simply following Röntgen's directions. Röntgen himself took no part in the ensuing race to develop practical applications for his discovery, although he used his apparatus to take an occasional photograph for his medical colleagues.[9]

THE PUBLIC

The discovery of x-rays stirred the interest of everyone. Its appeal was not limited to the physicists alone. Physicians, photographers, "electricians," and charlatans seized upon it and proceeded to exploit it, each to his own end. Public interest was expressed in cartoons, humorous verse, and advertisements for x-ray proof garments to preserve feminine modesty. Shoe stores featured x-ray photographs of feet cramped by poorly fitted shoes and x-ray machines for fitting shoes were soon put on the market. Edison gave a public demonstration of x-rays in New York City during March, 1896. Visitors were allowed to view their hands and arms under the fluoroscope, and the exhibit proved to be a great attraction.

> Professor Elihu Thomson, the well-known electrician, recently fractured the bone of his leg just above the ankle. "He has been an enthusiastic investigator of the Röntgen discovery," says the *Electrical Review*, and after the fracture was set had an x-ray picture taken of it. The result was very satisfactory, showing the surgical adjustment of the bone to be most perfect and only a fine line showing the break.[16]

This report, appearing in the *Literary Digest*, June 6, 1896, is representative of many similar reports concerning the use of x-rays in treating celebrities and even "the crowned heads of Europe," a much more impressive group then than now. Such extensive publicity resulted in a demand for x-ray

service on the part of patients. We are all aware of the pressure of public demand for a new drug or a new method of treatment which is fostered by articles in such magazines as the *Ladies' Home Journal* or the *Reader's Digest*. The people will be served. Physicians were subjected to an inexorable pressure to purchase the necessary equipment, and, willy-nilly, to begin using x-ray photographs as a regular part of their diagnostic armamentarium.

THE LAW

Patients with fractures, old and new, sought to have their injuries photographed by the new process. The taking of x-ray photographs was not always under the supervision of medical practitioners. Independent studios advertised and catered to the curious and disgruntled. The inevitable result was a rash of suits for malpractice against physicians. The situation was aggravated not only by the faulty technique which frequently distorted the photographs, but also by errors of interpretation due to inexperience. The first case tried in the United States in which x-rays were admitted as evidence was filed in Denver, April 14, 1896, and tried late in the fall.[27] The case involved a boy who had fallen from a ladder and injured his thigh. He consulted a surgeon who did not immobilize the limb, but treated him as for a contusion. X-ray examination later showed that the patient had fractured his femur. An Eastern judge had previously refused to admit x-rays in evidence in his court saying: "There is no proof that such a thing is possible. It is like offering the photograph of a ghost when there is no proof that there is any such thing as a ghost." However, Judge Owen LeFevre, in an opinion handed down, Dec. 2, 1896, admitted the x-rays in evidence and allowed them to be shown to the jury. Since that time juries have been impressed upon countless occasions by x-ray photographs of fractures, seeing with their own eyes if the bones were crooked or straight. The threat of legal action for malpractice based upon evidence provided by x-rays furnished, perhaps, the most potent stimulus for the rapid adoption of the routine use of x-rays in the treatment of fractures. More exact antaomic reduction of fractures became necessary, and the case for open reduction and internal fixation was strengthened.

It was soon apparent, however, that the appearance of the x-ray photograph did not provide a complete picture of the injury. The importance of viewing the patient as a whole was stressed by Dr. Rudolph Matas[14]:

> It is my opinion, based upon personal experience, that the practitioner cannot be held liable to damage in malpractice suits, simply on the x-ray evidence of imperfect union of fragments in cases of fractures. The criterion of deformity should not be the skiagraphic image, but the external appearance of the part as recognized by the naked eye; if the external appearance is good, there is no visible deformity and no imperfection in the limb from the functional point of view, then I would consider the result good, and the surgeon should not be charged with malpractice.

Juries, however, have remained impressionable. Since most fractures result from accidents which contain the seeds of a possible legal action, physicians,

for their own protection, were driven to adopt the routine use of x-rays in fracture cases.

THE MILITARY

The first serious investigation of the possible value of x-rays in diagnosis was carried out by the Prussian War Ministry. On Feb. 4, 1896, it was announced that a systematic study of anatomic and war surgery preparations in the pathologic museum was being carried out to determine if fractures and metallic foreign bodies could be demonstrated by this method.[17] The results of the investigation appeared late in 1896 in the form of a monograph.[25]

In April, 1896, the Army Medical Department of the British forces, having concluded that the value of x-rays was undisputed, took steps to supply an expedition into the Egyptian Sudan with x-ray equipment for use in the field.[18] Two complete sets of apparatus were sent up the Nile where they were used to localize foreign bodies and in the diagnosis and treatment of fractures. A report on the value of x-rays in localizing lodged bullets appeared in May, 1896, from an Italian Military Hospital at Naples engaged in treating soldiers wounded in Ethiopia.[19]

The Graeco-Turkish War of 1897 provided another convenient testing ground. The soldiers on both sides were supported by Red Cross medical units supplied with x-ray apparatus. In their reports,[1, 13] both the British Unit with the Greek Army and the German Unit with the Turkish Army emphasized the value of x-rays in the diagnosis of fractures and gunshot wounds. It was felt that x-ray facilities should be available in the first medical unit at which wounds could be properly examined and treated. Küttner[13] concluded a long discussion saying: "We possess a new aid in the x-ray which is so valuable, that the wounded have a right to have it employed in their care."

The medical department of our own army was not remiss in adopting the use of x-rays. During the war with Spain (1898) seventeen x-ray units were in use in general hospitals and upon hospital ships. A complete report of this accumulated experience was made in 1900: "The Use of the Röntgen Ray by the Medical Department of the United States Army in the War with Spain."[14] This profusely illustrated report showed the value of x-rays in diagnosing fractures by demonstrating their form, the amount of comminution, and the presence of foreign bodies, facts which could not have been easily determined by previously available methods.

The use of x-rays in the study of fractures and gunshot wounds led to an abrupt change in the methods of treating these injuries. The technique of localizing metallic foreign bodies was rapidly perfected. The number, size, and distribution of shell fragments and comminuted bony fragments could be determined with ease and accuracy. The probe, a badge of the military surgeon for centuries, was abandoned. It was soon recognized that all metallic foreign bodies could not be removed without the added trauma of an extensive exploration of the wound, and, what is more important, that it was not necessary to remove all of these fragments to obtain healing. A large amount of meddlesome surgery could be avoided.

These many reports attesting to the value of x-rays as a diagnostic aid in the treatment of war casualties encouraged civilian doctors to adopt the method and provided still another stimulus for its acceptance.

THE MEDICAL PROFESSION

As is the case with all innovations in medical practice, the exploitation of Röntgen's discovery was enthusiastically exposed by some, observed skeptically or ignored by many, and actively opposed by a few. One of the most enthusiastic was Henry W. Cattell of the University of Pennsylvania who as early as March 6, 1896, wrote in *Science*[6]:

> The manifold uses to which Röntgen's discovery may be applied in medicine are so obvious that it is even now questionable whether a surgeon would be morally justified in performing a certain class of operation without having first seen pictured by these rays, the field of his work, a map, as it were, of the unknown country he is to explore.

A Boston physician later in the same year expressed the opinion that no well-equipped hospital in the land could do justice to its patients unless it possessed a complete x-ray outfit.[22] Similar expressions of opinion were echoed from Baltimore[12] and St. Louis[5] and seemed to represent a spontaneous development of opinion throughout the country.

The voice of skepticism was raised in a leading editorial in *The Medical News,* Feb. 22, 1896:

> As far as our present knowledge goes, the positive advantages to medicine seem to be limited to three conditions; fractures, dislocations and tumors of bones, encysted bullets, needles or pieces of glass in the tissues, and earthy calculi. In the first class of conditions, its advantages would appear to be slight unless great advances upon present powers and methods can be made. The *Tactus eruditus* is certainly a delicate and reliable sense in investigating fractures and dislocations, and it is questionable how much help can be obtained by such crude and blurred shadow pictures as can at present be obtained. In recent cases of fracture or dislocation, the delay and discomfort to the patient necessarily involved in the application of the method would be practically an insuperable objection to its use for purposes of diagnosis. . . .

This skepticism as to the practical value of x-rays resulted from too great expectations and the failures and disappointments which necessarily attend the development of any new technique. And it persisted.

McCosh,[15] in the same journal in July, 1896, gave a résumé of the recent progress in the treatment of fractures, omitting all mention of the use of x-rays. The following year (1897) David W. Cheever in the Shattuck Lecture, "The New Surgery,"[7] hailed the advent of a great new epoch as a result of the development of anesthesia and antiseptic surgery, with no mention of Röntgen's discovery.

Bigelow's[3] famous book, *The Mechanism of Dislocations and Fracture of the Hip,* was reprinted in 1900 without the addition of a single x-ray photograph of these conditions, an addition which would have been of inestimable value. The following note from a review of the third edition (1901)

of Stimson's "A Practical Treatise on Fractures and Dislocations,"[21] is illustrative of the inertia characteristic of many "authorities."

> The plates added include a number of very interesting skiagrams, although the author rarely receives information of practical importance from the x-ray in fractures which could not be obtained by other means.

This attitude was reflected in the Report of the Committee of the American Surgical Association of the Medico-Legal Relations of the X-rays (1900). This most interesting document consists largely of complaints by the members who have been sued for malpractice on the basis of x-ray evidence. It concludes:

> The routine employment of the x-ray in cases of fractures is not at present of sufficient definite advantage to justify the teaching that it should be used in every case.[20]

The position of this august association was not officially reversed for thirteen years (1913), when its committee on fractures recommended the routine use of x-rays in all cases of fractures and dislocations.[24]

The first ten years following the discovery of x-rays was a time of trial and error. The incidence of burns, epilation, misinterpretation, and technical failures could not obscure the real value of the method in diagnosis. They produced, instead of discouragement, a stimulus to the development of improved equipment, and a greater understanding of both the normal and the anomalous anatomy as seen in the x-ray photograph. The value of x-rays in the treatment of fractures at the end of this period was epitomized by Walsh in 1907[26]:

> To sum up: in dealing with bone injuries successful radiography, compared with previous methods, offers the following advantages. It substitutes speed, accuracy, and finality for delay and doubt; it affords exact evidence that many confirm or modify the diagnosis of the surgeon; it may furnish both grounds for prognosis and hints for treatment; it may save the patient the pain of useless and perhaps dangerous manipulations, as well as the risk of anesthetics; it provides a permanent record of the precise nature of an injury; it may prove a safeguard for the patient and for his medical attendant, both in the present and the future, and lastly it has a special value for teaching purposes.

THE STUDENT

The development of the use of x-rays in the treatment of fractures wrought a fundamental change in the method of teaching students how to care for these injuries. Previously the student was fortunate if he could follow a few cases of fractures from the time of the accident until complete healing occurred. He was forced to rely upon the description of the clinical examination at various stages to provide a picture of the course of events during the healing period. X-ray photographs provided a permanent record of the patient's condition. Patients could be shown to students at any stage of their treatment, and their course reconstructed for the students by showing the antecedent x-ray photographs. Didactic diagrams of typical

fractures could be discarded in favor of x-ray photographs of actual fractures. This added greatly to the clinical atmosphere of the lecture room. The opportunity of observing the rarer varieties of fractures and dislocations became available to all, since the x-ray photographs of these occasional cases were preserved and used for teaching purposes. The most important feature of any program of teaching fracture treatment has become the clinical x-ray conference.

The need for new textbooks incorporating information about fractures gained by the use of x-rays was widely expressed as early as 1897.

> We were certainly justified in supposing that our knowledge of fractures had nearly reached its limit; but the Röntgen rays have opened up new fields for investigation, and we find that there is still much to learn. . . . a complete new set of data must now be accumulated and reviewed.[10]
>
> There will have to be a new treatise on fractures and dislocations, based upon the x-ray. There are many surprises in store, many surgical bugaboos will go, and many revelations will simplify much which is still obscure.[8]

In 1900 Carl Beck published his book, *Fractures, With an Appendix on the Practical Use of the Röntgen Rays,*[2] which was dedicated: "To Wilhelm Conrad Röntgen without whose discovery much of this book could not have been written." This was the first book on the diagnosis and treatment of fractures based upon the routine use of the x-rays, and is the prototype of all of our standard fracture texts today.

CONCLUSION

Röntgen's discovery of x-rays, and their rapid exploitation in medicine, has effected a great improvement in the treatment of patients with fractures. This is due to more accurate diagnosis and to an insistence upon a more exact anatomic reposition of the fragments. The speed with which the new method was developed and accepted, was the result of a combination of forces acting within and without the medical profession.

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Recent Advances in Surgery

CONDUCTED BY ALFRED BLALOCK, M.D.

EXPERIMENTAL VASCULAR GRAFTS: AN EVALUATION RELATING TO TYPES, MEANS OF PRESERVATION, AND METHODS OF SUTURE IN THE GROWING PIG

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THE successful treatment of patients, either directly or indirectly, is the basic goal of all worthy endeavor in the field of medicine, and especially is this true of vascular surgery. Certainly, it can be said that this has been the goal of all experimental study either of methods of vascular repair or of blood vessel replacements. The information obtained from these fundamental studies enabled surgeons, skilled in the techniques of vascular repair, to extend effective treatment to many patients who previously could not be aided. The story of these experimental findings and their subsequent clinical application comprises one of the most exciting chapters in medical history.

Vascular grafts have proved to be of clinical value by enabling the surgeon to correct or improve situations which otherwise were hopeless or unsatisfactory. There is much that remains to be learned of such grafts from both further experimental and clinical study. Few investigators have carefully studied more than one type of graft in sufficient numbers to allow for a comparison of the different types of grafts. It would seem desirable to be able to compare the results obtained with different types of grafts studied by the same investigators under similar conditions. In this report, we are presenting the results we have obtained from a study of different types of vascular grafts implanted in the abdominal aortas of 148 young pigs.

EXPERIMENTAL PROCEDURES AND RESULTS

One hundred and forty-eight young pigs, averaging 30 pounds in weight, were operated upon and a vascular graft implanted in the abdominal aorta of each. Thirty of these pigs died in the postoperative period from a variety of causes. One hundred and eighteen of the 148 pigs came to slaughter an average of 205 days after operation. At slaughter, these pigs averaged 240 pounds in weight. This gain represents an average increase in weight of those pigs coming to slaughter of 700 per cent.

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TABLE I. ONE HUNDRED FORTY-EIGHT VASCULAR GRAFTS IMPLANTED IN THE ABDOMINAL AORTA OF THE GROWING PIG: DURATION OF IMPLANTATION, WEIGHT CHANGES, AND GRAFT LENGTH CHANGES

TYPE OF GRAFT	FRESH AORTIC AUTOGRAFTS	FRESH AORTIC HOMO-GRAFTS	DELAYED AORTIC HOMO-GRAFTS	FRESH INFERIOR VENA CAVAL AUTOGRAFTS	DELAYED INFERIOR VENA CAVAL AUTOGRAFTS	FRESH INFERIOR VENA CAVAL HOMO-GRAFTS	DELAYED INFERIOR VENA CAVAL HOMO-GRAFTS	ALL GRAFTS
Number of pigs								
Operated	17	9	46	16	15	11	34	148
Slaughtered	14	9	35	12	13	8	27	118
Grafts open at slaughter	14	9	32	7	8	3	11	84
Average weight at operation of pigs having open grafts at slaughter	31	25	31	27	30	28	33	30
Average days from operation to slaughter of pigs with open grafts at slaughter	219	218	189	225	181	184	192	200
Average weight at slaughter of pigs with open grafts	274	252	238	252	217	197	239	236
Average per cent increase in weight at slaughter of pigs with open grafts	784	908	668	833	623	604	624	687
Average length (cm.) at operation of grafts open at slaughter	1.62	0.99	1.07	1.71	1.64	2.15	2.10	1.44
Average length (cm.) of grafts open at slaughter	3.2	2.20	1.86	3.75	2.31	3.50	2.65	2.49
Average per cent increase in length of grafts open at slaughter	98	122	74	119	41	63	24	73

The grafts employed in this study must be considered as short length grafts. They fall into seven different categories. In Table I the average duration of implantation, of pig weight change, and of graft length change in these 7 different groups are shown. In these experiments, both fresh and delayed grafts were studied. The delayed grafts had been preserved at 4° C. in light mineral oil, in Ringer's solution containing 10 per cent homologous serum, or in modified Tyrode's solution containing 10 per cent homologous serum (Gross, Bill, and Peirce, 1949) for varying periods prior to implantation. The following is an outline of the different types of grafts that were implanted:

A. Autograft
  1. Aortic
    a. Fresh—17 grafts
    b. Preserved—no grafts
  2. Inferior Vena Caval
    a. Fresh—16 grafts
    b. Preserved—15 grafts
      (1) in light mineral oil—5 grafts (preserved from 7 to 33 days)
      (2) in Ringer's solution—5 grafts (preserved from 6 to 33 days)
      (3) in Tyrode's solution—5 grafts (preserved from 8 to 28 days)

B. Homograft
  1. Aortic
    a. Fresh—9 grafts
    b. Preserved—46 grafts
      (1) in light mineral oil—19 grafts (preserved from 1 to 181 days)
      (2) in Ringer's solution—14 grafts (preserved from 1 to 126 days)
      (3) in Tyrode's solution—13 grafts (preserved from 1 to 120 days)
  2. Inferior Vena Caval
    a. Fresh—11 grafts
    b. Preserved—34 grafts
      (1) in light mineral oil—11 grafts (preserved from 1 to 81 days)
      (2) in Ringer's solution—13 grafts (preserved from 1 to 105 days)
      (3) in Tyrode's solution—10 grafts (preserved from 1 to 136 days)

At operation, anesthesia was accomplished by intraperitoneal Nembutal (60 mg. per 5 pounds of pig weight) with supplemental open drop ether. The abdominal aorta was exposed retroperitoneally through a flank incision and sufficient aorta removed to prevent tortuosity of the graft. Only when the inferior vena cava was to be resected was the approach made from the right side. In the delayed inferior vena caval autografts, the inferior vena cava was resected through a right flank incision, and after a storage period the graft was implanted in the aorta through a left flank incision. The anastomoses were performed by a variety of techniques using various sizes of silk or catgut. After implantation, measurements were taken of the graft length, of the external diameter of the graft, upper anastomosis, lower anastomosis, aorta midway between graft and a renal artery, and the aorta 1 cm. below the graft, and the distance from graft to renal artery. In addition, the crown-rump length of the pig and the length of the incision were measured.

A few days after surgery, the pigs were sent to a farm and kept until they weighed 200 pounds or more and then were slaughtered. The crown-

rump and incision lengths of the pigs were recorded. The abdominal aorta was removed and carefully dissected free from surrounding tissue with division and ligation of branches. The same measurements, previously taken at operation, were repeated after inflating the segment of aorta containing the graft to 120 mm. Hg with air. All measurements and dissections, both at the time of operation and slaughter (both in situ and after removal of the specimen), were taken by one of us (L. R. S.). In this respect, our observations are more complete and comparable than many of those reported by others. The dimensional changes in terms of per cent increase or decrease were then calculated. Measurements of the open vessel were also taken but were not considered as accurate as those of the inflated vessel. X-ray studies of Diodrast-filled grafts were made in some instances. All grafts, open at slaughter, were photographed both inflated and opened. These grafts were then sectioned for microscopic study and stained with hematoxylin and eosin, and Verhoeff's elastic tissue stain.

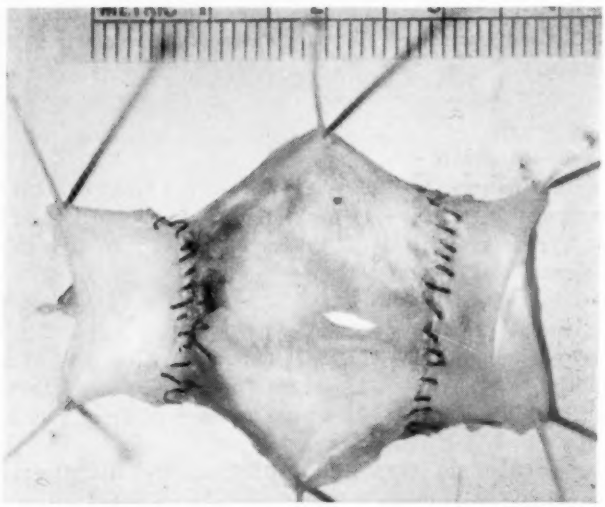


Fig. 1 (Pig 42).—This graft, a delayed inferior vena cava autograft, preserved 9 days in Ringer's solution prior to implantation, ruptured on the fifth postoperative day leading to death of the pig. Note that the rupture is in the graft proper and not at a suture line. The anastomoses were performed with continuous 00000 silk using the triangulation method of Carrel.

RUPTURE

As listed in Table II*A*, graft rupture occurred 4 times in the entire series. All ruptures occurred in venous grafts. In each instance, the site of rupture was toward the middle of the graft (Fig. 1). It could not be determined at post-mortem examination whether the rupture had occurred at the site of a previously ligated tributary or not. No instance of suture line dehiscence occurred in the entire series. Death occurred from rupture in a fresh inferior vena caval autograft, in a delayed inferior vena caval autograft preserved 9 days in Ringer's solution (Fig. 1), in a fresh inferior vena caval homograft, and in a delayed inferior vena caval homograft preserved 26 days in Tyrode's

solution on the fourth, fifth, twentieth, and nineteenth postoperative days, respectively.

THROMBOSIS*

Pigs showing evidence of aortic occlusion in the immediate postoperative period (paraplegia, incontinence, and cold hind legs) were classified as having immediate thrombosis of the graft. Autopsy findings confirmed this antemortem diagnosis. Other pigs had occluded grafts at the time of slaughter but, to our knowledge, either had never had evidence of circulatory insufficiency or had had only transient episodes of hind leg weakness. These grafts were classified as showing delayed thrombosis.

As shown in Table II*A*, the incidence of immediate or operative thrombosis with fresh and delayed grafts, the latter without reference to means of preservation, was highest (19 per cent) in the fresh inferior vena caval autografts. The incidence of delayed thrombosis was highest (55 per cent) in the fresh inferior vena caval homografts. The incidence of delayed thrombosis was much higher in the venous grafts, autogenous or homogenous, than it was in the arterial grafts.

TABLE II*A*. SUMMARY OF RESULTS IN ONE HUNDRED FORTY-EIGHT AORTIC AND INFERIOR VENA CAVAL GRAFTS IMPLANTED IN THE ABDOMINAL AORTA OF THE GROWING PIG

	AUTOGRAFTS						HOMOGRAFTS							
	FRESH				DELAYED		FRESH				DELAYED			
	AORTIC		CAVAL		CAVAL		AORTIC		CAVAL		AORTIC		CAVAL	
	NO.	% OF TOTAL	NO.	% OF TOTAL	NO.	% OF TOTAL	NO.	% OF TOTAL	NO.	% OF TOTAL	NO.	% OF TOTAL	NO.	% OF TOTAL
Immediate thrombosis	3	18	3	19	1	7	0	0	0	0	7	15	5	15
Delayed thrombosis	0	0	5	31	5	33	0	0	6	55	3	7	14	41
Rupture	0	0	1*	6	1†	7	0	0	1‡	9	0	0	1§	3
Dead from nonvascular causes	0	0	0	0	0	0	0	0	1	9	4	9	3	9
Grafts open at slaughter	14	*82*	7	*44*	8	*53*	9	*100*	3	*27*	32	*69*	11	*32*
Total grafts	17	100	16	100	15	100	9	100	11	100	46	100	34	100

*Death on fourth postoperative day.

†Death on fifth postoperative day. Graft preserved 9 days in Ringer's solution prior to implantation.

‡Death on twentieth postoperative day.

§Death on nineteenth postoperative day. Graft preserved 26 days in Tyrode's solution prior to implantation.

As shown in Table II*B*, the incidence of thrombosis in the delayed grafts preserved at 4° C. in various media (light mineral oil, Ringer's solution, or Tyrode's solution) was not greatly different. Considering together all grafts preserved in one type of media, the incidence of thrombosis (immediate and

*In no instance was heparin used in a graft which was open at the time of slaughter. In several instances, it was used when suggestive signs of thrombosis were observed, in all instances definite thrombosis being found at autopsy (early) or slaughter (late). It may be of interest that artificial aids to control leakage at the suture lines (Gelfoam, Oxycel, and others) were not used in these studies.

TABLE II*B*. RELATION OF MEANS OF PRESERVATION TO INCIDENCE OF THROMBOSIS IN DELAYED GRAFTS

	PRESERVED INFERIOR VENA CAVAL GRAFTS										PRESERVED AORTIC HOMOGRAFTS					TOTAL GRAFTS		
	AUTOGENOUS					HOMOGENOUS												
		THROMBOSIS					THROMBOSIS					THROMBOSIS						
		IMMEDIATE		DELAYED			IMMEDIATE		DELAYED			IMMEDIATE		DELAYED				
PRESERVED IN	NO. OF GRAFTS	NO.	% OF TOTAL	NO.	% OF TOTAL	NO. OF GRAFTS	NO.	% OF TOTAL	NO.	% OF TOTAL	NO. OF GRAFTS	NO.	% OF TOTAL	NO.	% OF TOTAL	NO.	NO. THROM-BOSED	% THROM-BOSED
Light mineral oil	5	0	0	3	60	11	2	18	5	45	19	3	16	1	5	35	14	40
Ringer's solution	5	0	0	1	20	13	3	23	6	46	14	3	21	0	0	32	13	41
Tyrode's solution	5	1	20	1	20	10	0	0	3	30	13	1	8	2	15	28	8	28
Total	15	1	7	5	33	34	5	15	14	41	46	7	15	3	7	95	35	37

delayed combined) for grafts preserved in light mineral oil (35), in Ringer's solution (32), or in Tyrode's solution (28) was 40, 41, and 28 per cent, respectively.

Although not adequately reflected in the statistics, venous grafts were poorly preserved in light mineral oil at 4° C. as compared to similar grafts in Ringer's or in Tyrode's solution. Venous grafts preserved longer than two months in mineral oil tended to become soft, oily, and gelatinous. These changes in the graft made suturing exceedingly difficult. One graft preserved 90 days in mineral oil could not be sutured because of its formless oily character. Both of the mineral oil venous grafts implanted after more than 54 days of storage thrombosed. Undoubtedly, had it been possible to implant older grafts, the incidence of immediate thrombosis would have been very high in this group. Venous grafts preserved in Ringer's or in Tyrode's solution were still of excellent quality after more than 100 days of preservation.

Arterial grafts, on the other hand, could be preserved for long periods at 4° C. in light mineral oil and still be sutured easily. However, as with veins but to a much lesser extent, these grafts were not of the same quality as similar grafts preserved in Ringer's or in Tyrode's solution. After several months of storage in mineral oil, the arterial grafts tended to become soft.

Except in the case of the venous grafts preserved in mineral oil, we did not feel that we had extended the storage period of these vessels to their upper limit of successful usability as vascular grafts. In fact, the results of those grafts preserved longer than 100 days prior to implantation would suggest that the storage period for the methods employed was far from the upper limit. None of three venous grafts preserved longer than 100 days thrombosed. The arterial grafts preserved for the longest periods (120 days in Tyrode's solution, 126 days in Ringer's solution, 150 days in light mineral oil, and 181 days in light mineral oil), all remained patent. The incidence of thrombosis for all grafts preserved longer than 100 days was 17 per cent (2 of 12). This compares favorably with an incidence of thrombosis for all grafts preserved less than 100 days of 40 per cent (33 of 83).

GROSS APPEARANCE

Only in the case of the aortic autografts was there difficulty in distinguishing between the graft and the aorta at the time of slaughter. Except for the presence of suture lines, these grafts resembled the aorta in all obvious respects (Fig. 2). Only 1 of 41 aortic homografts open at slaughter, including 9 fresh grafts, resembled an aortic autograft. This graft (Fig. 3), an aortic homograft preserved one day in Tyrode's solution prior to implantation in a nonlitter mate pig, possessed normal elasticity and resembled the aorta very closely. The other 40 aortic homografts (Figs. 4 to 10), including all the fresh grafts, were inelastic. In most instances, they were thin-walled and pliable. The internal linings of the grafts, though often uneven, were smooth and covered both suture lines. These grafts were all smaller than the aortas at time of slaughter.

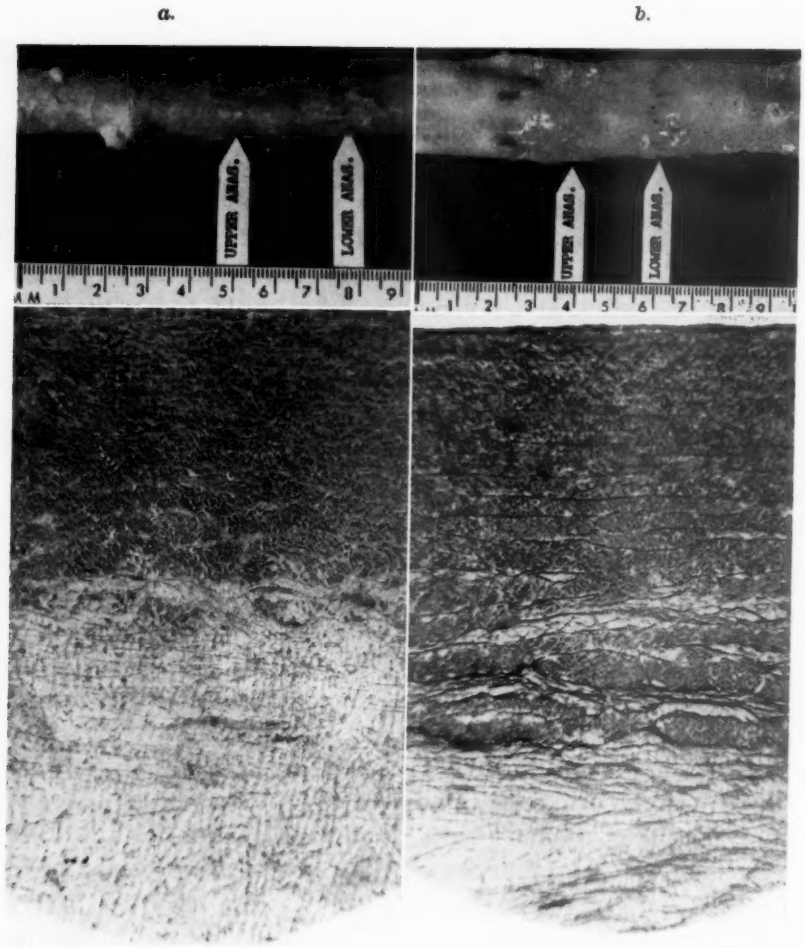


Fig. 2 (Pig 163 [36]).—This fresh aortic autograft has been in place for 230 days with a pig weight increase of 967 per cent. The upper anastomosis was performed with continuous 00000 catgut using the everting mattress method; the lower anastomosis was performed with 00000 silk, the posterior row with continuous, the anterior row with 7 interrupted Carrel sutures. The graft length, distance from graft to left renal artery, crown-rump length, and incision length increased 100, 74, 86, and 99 per cent, respectively. Dimensional changes were: (1) the exterior diameter aorta 1 cm. above the graft, 164 per cent increase, (2) the exterior diameter of the upper anastomosis, 160 per cent increase, (3) the exterior diameter of the graft, of 170 per cent increase, (4) the exterior diameter of the lower anastomosis, 160 per cent increase, (5) the exterior diameter of the aorta 1 cm. below the graft, 170 per cent increase.

a, There is no constriction either of the graft or of the anastomoses. The continuous catgut suture of the upper anastomosis has been absorbed. The interrupted stitches of the lower anastomosis, close together at operation, are now widely separated.

b, The surface of the graft is smooth and even. The majority of the growth of the lower anastomosis took place in the area approximated with interrupted stitches.

c, The graft shows normal arterial cellular architecture.

d, The elastic tissue of the graft is distributed between the smooth muscle cells of the media. This graft classifies as satisfactory. (See Table III.)

In all the figures of graft specimens removed at slaughter in this paper, *a* is a photograph of the graft inflated to 120 mm. Hg with air, *b* is a photograph of the graft opened in the long axis of the vessel and viewed from the intimal side, *c* is a photomicrograph of a longitudinal section of the graft (hematoxylin and eosin stain), and *d* is approximately the same section as *c* but with Verhoeff's elastic tissue stain. The scale in *a* and *b* is in centimeters. All photomicrographs are ×60.

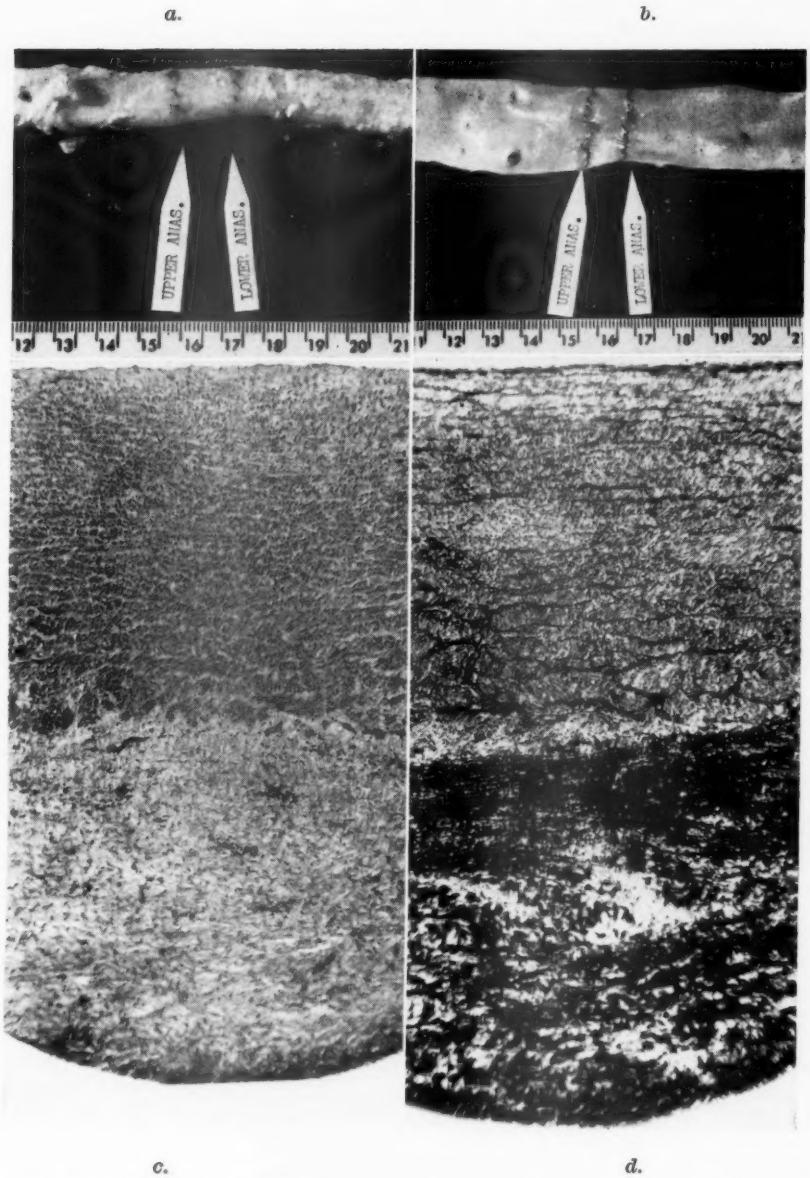


Fig. 3 (Pig 64 [45]).—This aortic homograft, previously stored 1 day in Tyrode's solution, has been in place for 195 days in the abdominal aorta of a nonlitter mate pig, with a pig weight increase of 995 per cent. Both anastomoses were performed with continuous 00000 silk using the Carrel method. Dimensional changes were: (1) graft length, 133 per cent increase, (2) graft diameter, 77 per cent increase, (3) diameter of upper anastomosis, 118 per cent increase, (4) diameter of lower anastomosis, 100 per cent increase, (5) distance from graft to right renal artery, 142 per cent increase, (6) diameter of aorta 2 cm. above graft, 188 per cent increase, (7) diameter of aorta 2 cm. below graft, 188 per cent increase.

a, There is no significant constriction of this graft which possessed normal elasticity at the time of slaughter. The continuous silk sutures, used for the anastomoses, have not completely straightened even though the upper anastomosis increased 118 per cent and the lower 100 per cent.

b, The surface of the graft is smooth and even.

c, The graft shows normal arterial cellular architecture.

d, Elastic tissue is present in moderate amounts between the smooth muscle cells of the media and in large amounts in the adventitia. This graft classifies as satisfactory.

The fresh inferior vena caval autografts varied considerably in appearance, some being dilated (Fig. 11), others being only slightly larger, and others being slightly smaller than the aorta (Fig. 12). These grafts were inelastic, pliable, and often had walls considerably thicker than the aorta, except in instances of dilatation where the dilated area had a thinner wall than the rest of the graft.

Seven of 8 delayed inferior vena caval autografts, of which the specimen from Pig 90(67) as shown in Fig. 13 is an illustrative example, resembled

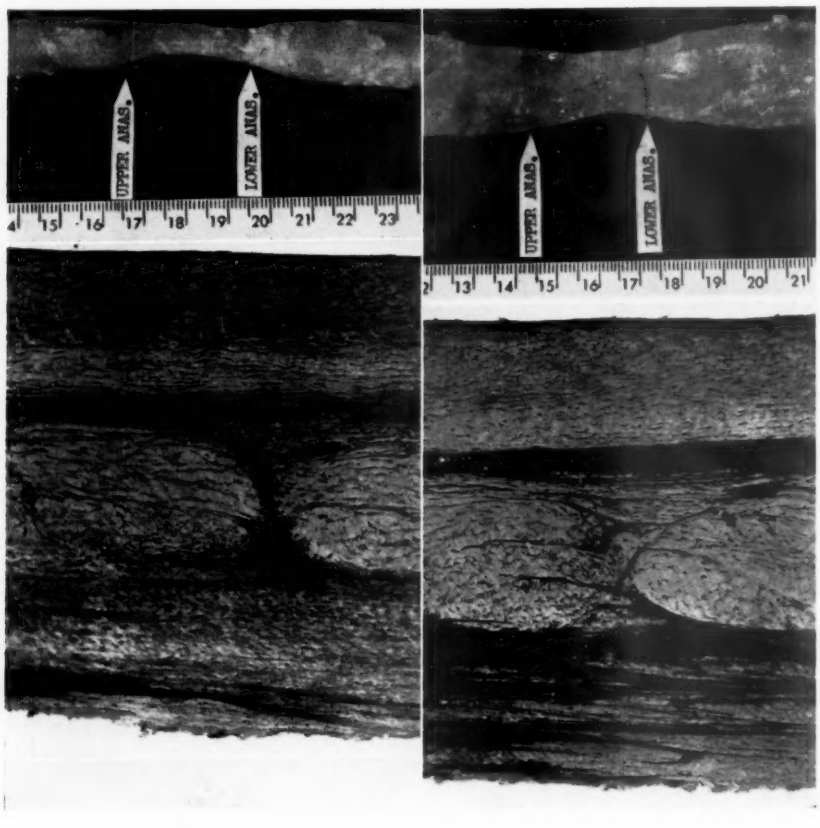


Fig. 4 (Pig 123 [98]).—This fresh aortic homograft has been in place in a nonlitter mate for 239 days with a pig weight increase of 825 per cent. The upper anastomosis was performed with continuous 00000 catgut using the Carrel method, and the lower anastomosis in the same manner with 00000 silk. Dimensional changes were: (1) crown-rump length, 88 per cent increase, (2) graft length, 71 per cent increase, (3) graft diameter, 18 per cent increase, (4) diameter of upper anastomosis, 110 per cent increase, (5) diameter of lower anastomosis, 50 per cent increase, (6) distance from graft to left renal artery, 70 per cent increase, (7) diameter of aorta 1 cm. above graft, 109 per cent increase, (8) diameter of aorta 3 cm. below graft, 146 per cent increase.

a, There is definite constriction of the graft, it being 43 per cent smaller than the aorta 1 cm. above the graft.

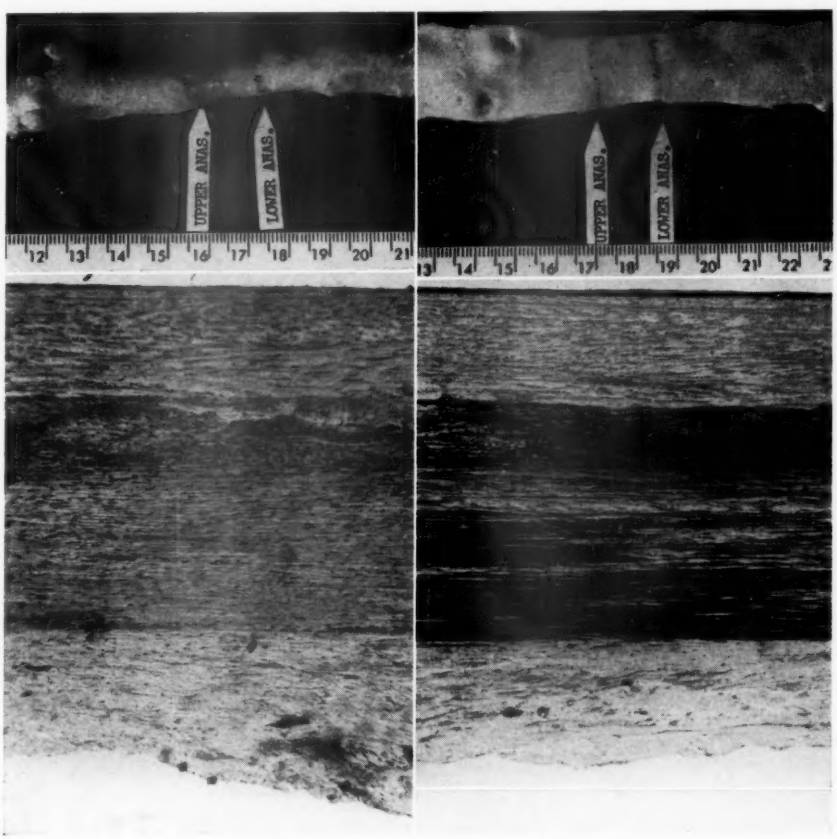
b, The intimal surface is smooth and even. With only a 50 per cent increase in the external diameter of the lower anastomosis, the continuous 00000 silk suture employed as an end-on coaptation stitch has practically completely straightened. This implies that the stitches were placed very close to the vessel edge.

c, No smooth muscle cells are visible. The wall is composed of connective tissue lined internally by endothelium.

d, The elastic tissue is condensed into 2 sheets, 1 lying in the middle and the other in the outer portion of the wall. This graft classifies as unsatisfactory on the basis of stenosis.

Fig. 5*A*.—The photograph was taken at the time of implantation of this aortic homograft (in Pig. 102 [78]) which had been stored in light mineral oil for 1 day. Its length measured 0.95 cm. The upper anastomosis is to the right and the lower anastomosis to the left.

a. *b.*



c. *d.*

Fig. 5*B* (Pig 102 [78]).—This is the same graft as shown in Fig. 5*A*, but after being in place in a litter mate for 237 days with a 767 per cent increase in pig weight. Both anastomoses were performed with continuous 00000 silk, using the Carrel method. Dimensional changes were: (1) crown-rump length, 79 per cent increase, (2) graft length, 58 per cent increase, (3) graft diameter, 50 per cent increase, (4) diameter of upper anastomosis, 82 per cent increase, (5) diameter of lower anastomosis, 58 per cent increase, (6) distance from graft to left renal artery, 60 per cent increase, (7) diameter of aorta 2 cm. above graft, 140 per cent increase, (8) diameter of aorta 2 cm. below graft, 140 per cent increase.

a, There is no significant constriction of the graft.

b, The inner surface is smooth and glistening. The upper suture has straightened more than the lower.

c, The graft shows absence of smooth muscle cells and is composed of dense connective tissue lined internally by endothelium.

d, The elastic tissue is condensed and in its inner portion is fragmented. This graft classified as partially satisfactory.

aortic homografts much more than they did fresh inferior vena caval autografts or inferior vena caval homografts, fresh or delayed. The eighth graft, preserved 7 days in light mineral oil prior to implantation, was dilated at the time of slaughter.

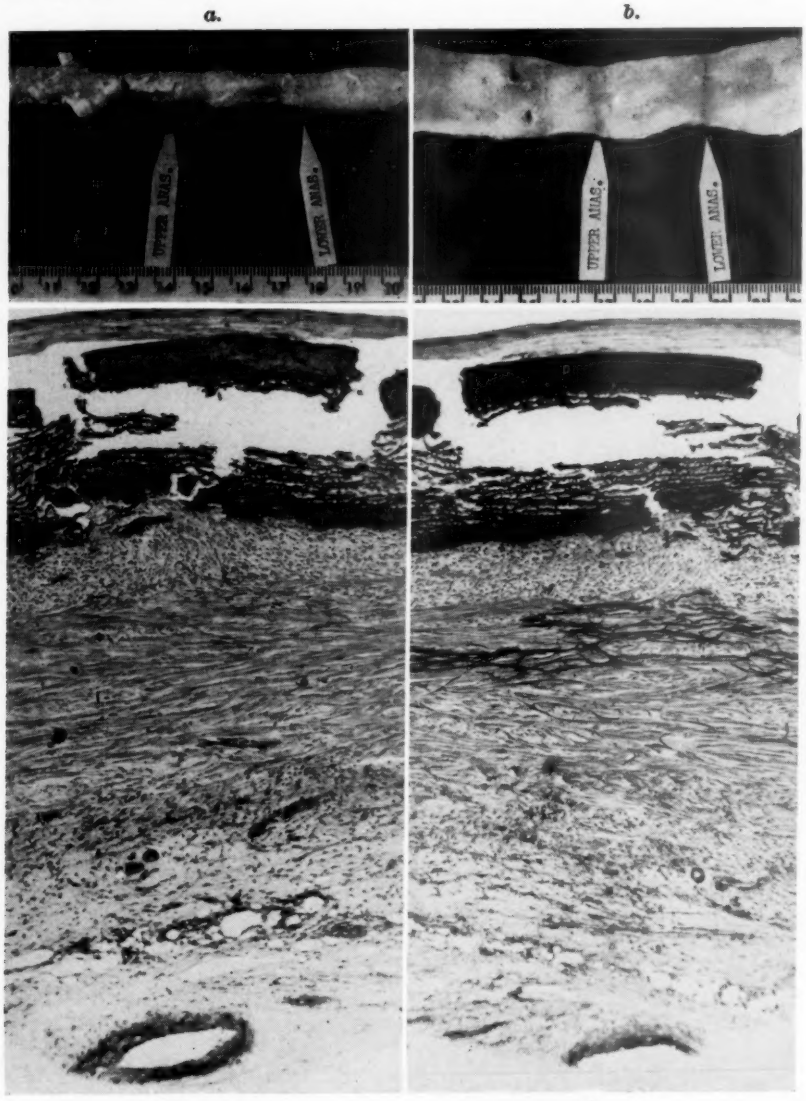


Fig. 6 (Pig 81 [60]).—This aortic homograft, previously stored for 101 days in light mineral oil, has been in place in a nonlitter mate for 165 days with a pig weight increase of 567 per cent. At implantation, its length was 2.80 cm., and its external diameter measured 50 per cent greater than that of the aorta. The upper anastomosis was performed with continuous 00000 catgut using the Carrel method, and the lower anastomosis in the same manner with 00000 silk. Dimensional changes were: (1) graft length, 11 per cent increase, (2) graft diameter, 22 per cent decrease, (3) diameter of upper anastomosis, 46 per cent increase, (4) diameter of lower anastomosis, 46 per cent increase, (5) distance from graft to left renal artery, 115 per cent increase, (6) diameter of aorta 2 cm. above graft, 83 per cent increase, (7) diameter of aorta 2 cm. below graft, 150 per cent increase.

a, Except for the ends, the walls of the graft are very hard and brittle and cannot be compressed without fracturing.

b, The inner surface is rough due to subendothelial deposits of thin sheets of brittle material which cracks audibly when broken.

c, Degenerative changes are seen in the wall near the inner surface of the graft.

d, These changes have occurred about the elastic tissue remnants of the original graft. This graft classifies as unsatisfactory on the basis of calcification.

The inferior vena caval homografts (Figs. 14 to 16), fresh or preserved, at time of slaughter were inelastic and, in most instances, had thicker walls than aortic homografts. Often there were tough thick areas in their walls which produced definite circumferential encroachment on the lumen.

HISTOLOGIC CHANGES

The anastomoses of all grafts had similar histologic findings. There was loss of smooth muscle cells and elastic tissue fibers. The anastomotic region

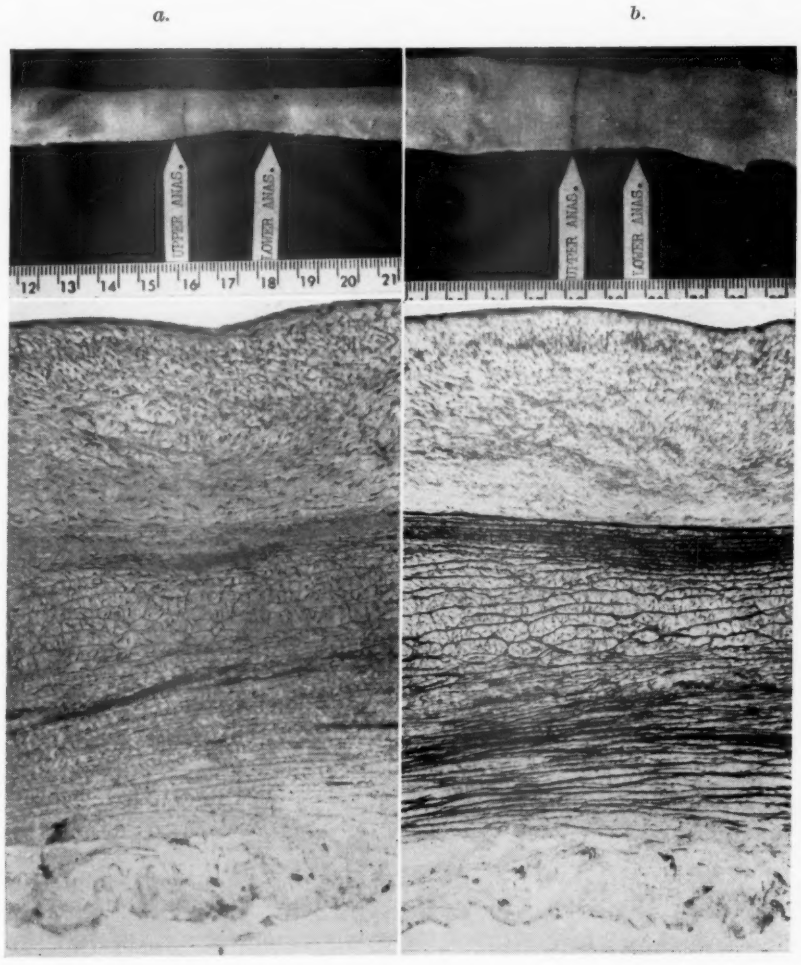


Fig. 7 (Pig 120 [95]).—This aortic homograft, previously stored 104 days in Tyrode's solution, has been in place in a nonlitter mate for 187 days with a 663 per cent increase in pig weight. The upper anastomosis was performed with continuous 00000 silk using the Carrel method, and the lower anastomosis with continuous 00000 catgut in the same manner. Dimensional changes were: (1) crown-rump length, 79 per cent increase, (2) graft length, 68 per cent increase, (3) graft diameter, 63 per cent increase, (4) diameter of upper anastomosis, 91 per cent increase, (5) diameter of lower anastomosis, 90 per cent increase, (6) distance from graft to left renal artery, 106 per cent increase, (7) diameter of aorta 2 cm. above graft, 130 per cent increase, (8) diameter of aorta 3 cm. below graft, 130 per cent increase.

a, There is no significant constriction of the graft. The continuous silk suture of the upper anastomosis has nearly straightened, but there is no anastomotic constriction.

b, The inner surface of the graft is smooth and glistening..

c, The wall is composed of fairly heavy connective tissue lined internally by endothelium.

d, The elastic tissue of the original graft is well preserved. This graft classifies as partially satisfactory. It is capable of serving as an effective conduit for the passage of blood.

was composed of connective tissue (fibroblasts and collagen fibers) lined internally by endothelium.

Contrary to the anastomoses, the grafts differed in their histologic findings. There was complete preservation of cellular integrity in each of the aortic autografts (Fig. 2), but cellular integrity was preserved in only one of the aortic homografts (Fig. 3). Apart from calcific changes (Fig. 6), the other aortic homografts (Figs. 4 to 10), fresh or preserved, had similar histologic fates, each becoming a connective tissue tube with an endothelial lining. While the smooth muscle cells disappeared, the elastic tissue fibers of the original graft persisted. At the time of slaughter, these fibers were in a variable state of organization which could not be correlated with the age of the graft at implantation.

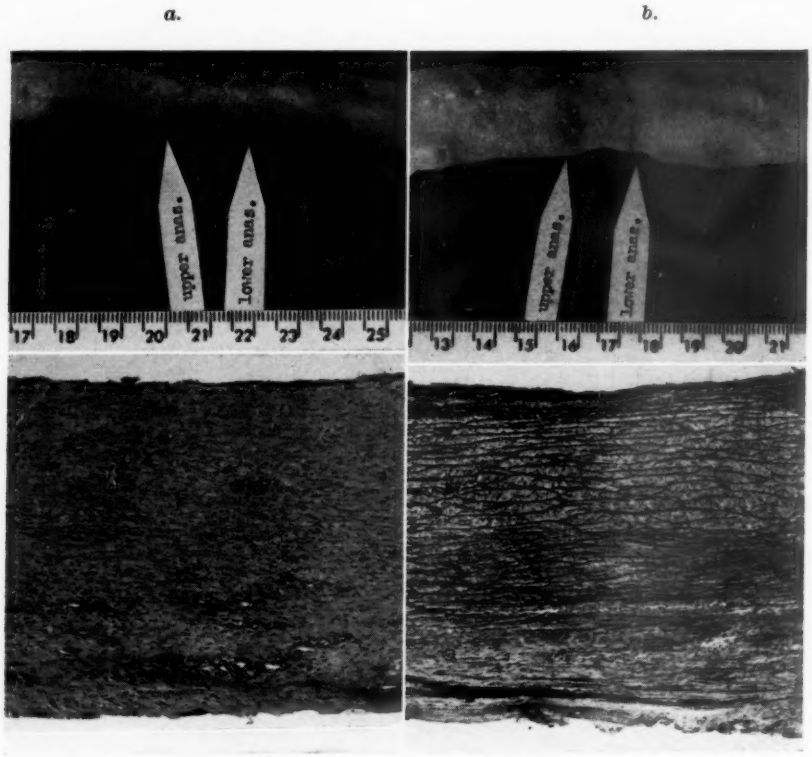


Fig. 8 (Pig 112 [88]).—This aortic homograft, previously stored in Ringer's solution for 105 days, has been in place in a nonlitter mate for 155 days with a pig weight increase of 600 per cent. The upper anastomosis was performed with continuous 00000 catgut using the Carrel method, and the same procedure was used for the lower anastomosis with 00000 silk. Dimensional changes were: (1) graft length, 50 per cent increase, (2) graft diameter 50 per cent increase, (3) diameter of upper anastomosis, 92 per cent increase, (4) diameter of lower anastomosis, 67 per cent increase, (5) distance from graft to left renal artery, 100 per cent increase, (6) diameter of aorta 2 cm. above graft, 79 per cent increase, (7) diameter of aorta 2 cm. below graft, 150 per cent increase.

a, There is moderate constriction of the graft but not sufficient to classify it as stenosed.

b, The inner surface is smooth and even.

c, The wall shows absence of smooth muscle cells and is composed of dense connective tissue.

d, The elastic tissue of the original graft is distributed throughout the wall. This graft classifies as partially satisfactory.

The constituents of the fresh and delayed inferior vena caval autografts and homografts (Figs. 11 to 5) were similar. These consisted of fibroblasts and collagen fibers. A much smaller though variable number of elastic tissue fibers also were present. Smooth muscle cells could not be identified at the time of slaughter. Calcific change was observed (Fig. 14) in only one instance in the venous grafts, this occurring in a fresh inferior vena caval homograft implanted in a litter mate pig.

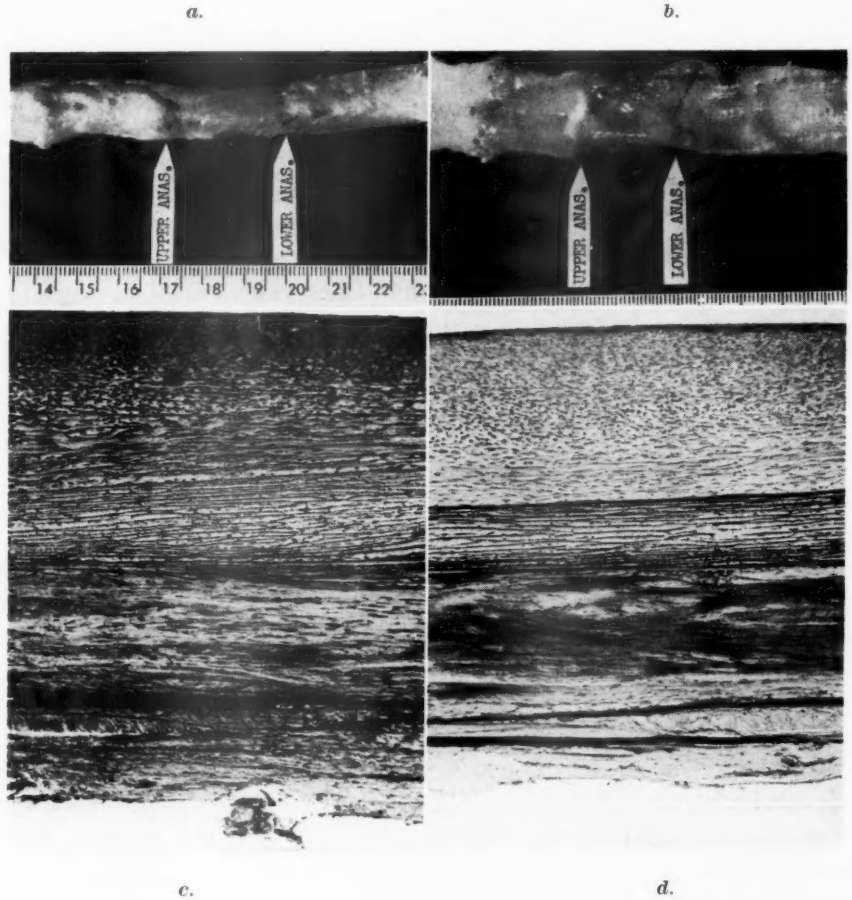


Fig. 9 (Pig 121 [96]).—This aortic homograft, previously stored in light mineral oil for 150 days, has been in place in a nonlitter mate for 243 days with a pig weight increase of 540 per cent. This graft is from the same donor vessel and kept in the same storage bottle as the graft shown in Fig. 6. The length of this graft at implantation was 1.20 cm. Both anastomoses were performed with continuous 00000 silk using the Carrel method. Dimensional changes were: (1) crown-rump length, 74 per cent increase, (2) graft length, 108 per cent increase, (3) graft diameter, 67 per cent increase, (4) diameter of upper anastomosis, 82 per cent increase, (5) diameter of lower anastomosis, 82 per cent increase, (6) distance from graft to left renal artery, 67 per cent increase, (7) diameter of aorta 2 cm. above graft, 65 per cent increase, (8) diameter of aorta 3 cm. below graft, 86 per cent increase.

a, There is no significant constriction of the graft.

b, There is definite constriction at the upper anastomosis due to an internal septum about 2.5 mm. high which projects into the lumen. The silk suture of the upper anastomosis is intact and straight. It lies in the middle of this septum and is covered by about 1 mm. of tissue. It is probable that the suture bites of the lower anastomosis were placed farther back from the vessel edge than was the case in the upper anastomosis. The inner surface of the graft proper is smooth and even.

c, The wall is composed of dense connective tissue lined internally by endothelium.

d, The elastic tissue is located in the middle of the wall. This graft classifies as partially satisfactory.

TABLE III. CRITERIA FOR CLASSIFICATION OF RESULTS OF VASCULAR GRAFTS OPEN AT SLAUGHTER

1. Satisfactory—Graft resembles the recipient vessel in all obvious respects both grossly and microscopically.
2. Partially Satisfactory—Although not resembling the recipient vessel in all obvious respects, there is no degenerative change (calcification or atheromatous plaques), dilatation, or stenosis.
3. Unsatisfactory—Graft shows degenerative change, dilatation, or stenosis alone or in combination.

CLASSIFICATION OF RESULTS

We have classified the results observed of those grafts open at slaughter as satisfactory, partially satisfactory, or unsatisfactory according to the criteria listed in Table III.

In the study of the dimensional changes of the grafts (Figs. 17 to 22), we have compared the external radius or diameter of the graft with the external radius or diameter of the aorta at the mid-point between the graft and the renal artery. In considering whether a graft is dilated or stenosed at the time of slaughter, one must take into account what the graft-recipient vessel caliber relationship was at the time of implantation. For the graft to be considered as dilated or stenosed at slaughter, there must be change in the rate of dimensional change of the graft as compared to that of the aorta.

If a graft were the same size or larger than the aorta at implantation, it is classified as stenosed and hence as unsatisfactory if its smallest external diameter at slaughter is as much as 40 per cent less than that of the aorta at the mid-point between the graft and the renal artery. Also, a graft of such size at operation is classified, under certain conditions, as stenosed at slaughter even though its smallest external diameter is not as much as 40 per cent less than that of the aorta at the mid-point between the graft and the renal artery. These conditions are that the graft has a tough, thick, fibrous constriction in its wall and the aorta below has increased in diameter as much as 100 per cent more than the aorta above the graft. The external diameter indicates that the internal diameter can be no greater, but it does not indicate how much smaller it may be. This is dependent upon the thickness of the vessel wall. If a graft were smaller than the aorta at implantation, it is not classified as stenosed at slaughter unless the graft-aortic diameter ratio has decreased as much as 40 per cent from the time of operation to slaughter.

If a graft were the same size or smaller than the aorta at implantation, it is classified at slaughter as dilated and hence as unsatisfactory if its largest external radius is as much as 40 per cent greater than that of the aorta at the mid-point between the graft and the renal artery. The radius of the graft is measured from a line joining the mid-point of the upper and lower anastomoses to the periphery. If a graft were larger than the aorta at operation, it is not classified as dilated at slaughter unless the per cent difference between the external radius of the graft and of the aorta has increased by at least 40 per cent from time of operation to slaughter.

As seen in Table IV, each of the 6 fresh aortic autografts whose dimensions were not influenced by the method of suture gave satisfactory results (Fig. 2).

One of 41 or 2.4 per cent of the aortic homografts (Fig. 3) gave a satisfactory result.

As shown in Tables IV and V, the highest percentage (81) of partially satisfactory results was obtained with the delayed aortic homografts. The preservative fluid did not appear to influence significantly the percentage of partially satisfactory results. The aortic homografts preserved in light mineral oil, in Ringer's solution, or in Tyrode's solution gave partially satisfactory results in 75, 91, and 78 per cent of instances, respectively. However, the inferior vena caval homografts preserved in light mineral oil, in Ringer's solution, or in Tyrode's solution gave partially satisfactory results in 67, 33, and 40 per cent of instances, respectively. Fifty-seven per cent of fresh and 75 per cent of delayed inferior vena caval autografts gave partially satisfactory results. Sixty-seven per cent of fresh aortic homografts and zero per cent of fresh inferior vena caval homografts gave partially satisfactory results.

DEGENERATAVE CHANGES

By degenerative changes we do not refer to the loss of cellular integrity of the vascular homograft (a normal occurrence) but rather to the development of atheromatous plaques or calcification in its wall. Among the grafts open at slaughter, there were 3 instances of degenerative changes. These changes occurred in 2 delayed aortic homografts and 1 fresh inferior vena caval homograft. These grafts were classified as unsatisfactory because of the presence of calcification in their walls located about the remnants of the original grafts. At the time of slaughter, small amounts of calcium were present in the wall of an aortic homograft which had been preserved 126 days in Ringer's solution prior to implantation. Extensive calcification was present in the wall of an aortic homograft (Fig. 6) preserved 101 days in mineral oil prior to implantation. It is of great interest that degenerative changes did not occur in segments of this same vessel stored in the same bottle of mineral oil for 150 and 181 days before implantation in the abdominal aortas of 2 other pigs (Figs. 9 and 10). Marked calcification occurred in a fresh inferior vena caval homograft (Fig. 14) implanted in the abdominal aorta of a litter mate pig. Degenerative changes were not observed in 2 other fresh inferior vena caval homografts or in 11 delayed grafts preserved from 16 to 105 days prior to implantation. Considering arterial and venous homografts together, both fresh and preserved, 3 of 55 showed degenerative changes at the time of slaughter, an incidence of 5.5 per cent.

GROWTH CHANGES

The average length changes of the different types of grafts are listed in Table I. In general, the graft length tended to increase at about the same rate as the aorta or the crown-rump length of the pig. In 6 months, a 30 pound pig will usually increase in weight from 600 to 800 per cent and in crown-rump length from 80 to 100 per cent. The incision length of the pig increased at roughly the same rate as the crown-rump length. The only grafts which differed markedly in their length change percentages (i.e., the length change

TABLE IV. CLASSIFICATION OF RESULTS OF SEVENTY-SIX AORTIC AND INFERIOR VENA CAVAL GRAFTS IMPLANTED IN THE ABDOMINAL AORTA OF THE GROWING PIG OPEN AT SLAUGHTER*

	AUTOGRAFTS						HOMOGRAFTS							
	FRESH				DELAYED		FRESH				DELAYED			
	AORTIC		CAVAL		CAVAL		AORTIC		CAVAL		AORTIC		CAVAL	
	NO.	% OF TOTAL	NO.	% OF TOTAL	NO.	% OF TOTAL	NO.	% OF TOTAL	NO.	% OF TOTAL	NO.	% OF TOTAL	NO.	% OF TOTAL
Total open grafts	6†	100	7	100	8	100	9	100	3	100	32	100	11	100
Satisfactory	6	*100*	0	0	0	0	0	0	0	0	1	3	0	0
Partially satisfactory	0	0	4	*57*	6	*75*	6	*67*	0	*0*	26	*81*	5	*45*
Unsatisfactory														
Degenerative change	0	0	0	0	0	0	0	0	1	33	2	6	0	0
Stenosis	0	0	0	0	1	12.5	3	33	2	67	3	10	6	55
Dilatation	0	0	3	43	1	12.5	0	0	0	0	0	0	0	0
Total unsatisfactory open grafts	0	*0*	3	*43*	2	*25*	3	*33*	3	*100*	5	*16*	6	*55*

*The delayed grafts shown in this Table were preserved at 4° C. in light mineral oil, in Ringer's solution containing 10 per cent homologous serum, or in Tyrode's solution also containing 10 per cent homologous serum. In Table V, only the delayed homografts preserved in mineral oil are analyzed.

†Does not include 8 grafts whose dimensions were influenced by the method of suture.

TABLE V. SUMMARY OF RESULTS IN THIRTY DELAYED AORTIC AND INFERIOR VENA CAVAL HOMOGRAFTS (PRESERVED IN LIGHT MINERAL OIL AT 4° C.) IMPLANTED IN THE ABDOMINAL AORTA OF THE GROWING PIG

DELAYED HOMOGRAFTS PRESERVED IN LIGHT MINERAL OIL	TOTAL GRAFTS	IMMEDIATE THROMBOSIS	DELAYED THROMBOSIS	RUPTURE	DEAD FROM NONVASCULAR CAUSES	TOTAL GRAFTS OPEN AT SLAUGHTER	GRAFTS OPEN AT SLAUGHTER							
							TOTAL	PRESERVATION OF CELLULAR INTEGRITY	CLASSIFICATION					TOTAL UNSATISFACTORY GRAFTS
									SATISFACTORY	PARTIALLY SATISFACTORY	UNSATISFACTORY			
											DEGENERATIVE CHANGE	STENOSIS	DILATATION	
Aortic														
Number	19	3	1	0	3	12	12	0	0	9	1	2	0	3
Per cent of total	100	16	5	0	16	*63*	100	0	*0*	*75*	8	17	0	*25*
Caval														
Number	11	2	5	0	1	3	3	0	0	2	0	1	0	1
Per cent of total	100	18	45	0	9	*27*	100	0	*0*	*67*	0	33	0	*33*

was less than in the other types) from the crown-rump length percentage increases were the delayed inferior vena caval autografts (average, 41 per cent increase) and the delayed inferior vena caval homografts (average, 24 per cent increase).

As shown in Figs. 17*A* and 18*A*, the aortic homografts (fresh or preserved) had similar caliber changes from time of operation to slaughter. These grafts, with one exception (Fig. 6), all increased in external diameter from time of operation to slaughter. However, only 1 (Fig. 9) increased at a rate faster than the aorta. The 3 grafts preserved in mineral oil for the longest periods (101, 150, and 181 days) were segments of the same donor vessel. The segment preserved for the shortest period, 101 days (Fig. 6), actually decreased in external diameter from time of operation to slaughter. The segment preserved for 150 days (Fig. 9) increased at a rate slightly greater than did the aorta. The segment preserved for 181 days (Fig. 10, *A* and *B*) increased at a rate approximately 75 per cent that of the aorta. These aortic homografts (both fresh and preserved), being approximately the same size as the aorta at implantation, as a consequence of their reduced rate of growth (one exception), were all smaller than the aorta at time of slaughter (Figs. 17*B* and 18*B*).

Fig. 10*A*.—The photograph was taken at the time of implantation (in Pig 146 [21]) of this aortic homograft which had been stored in light mineral oil for 181 days. Its length measured 0.95 cm. The upper anastomosis, performed with catgut, is to the right, and the lower anastomosis, performed with silk, to the left. This graft is from the same donor vessel and kept in the same storage bottle as the grafts shown in Figs. 6*A*, 6*B*, and 9.

As shown in Figs. 19*A* and 20*A*, preservation appeared to alter the dimensional changes of the inferior vena caval autografts. The dimensional changes of the fresh inferior vena caval autografts were variable. Of the 7 grafts studied, 3 increased much faster than the aorta, 2 at approximately the same rate, and the other 2 at a slower rate than the aorta. On the other hand, of the 8 delayed inferior vena caval autografts, 7 increased at a rate slower than the aorta, while only 1 increased at a rate faster than the aorta. It will be noticed that the percentage increase in the aortic diameter was less in the delayed autografts than in the fresh. This is related to the fact that at the time of implantation of the grafts, the walls of the aorta were thickened by a fibrous reaction subsequent to the operative manipulations of resecting the inferior vena cava at the preceding

operation. Thus the aortic measurements were larger than the true size of the aorta. This minimized the per cent increase in the aortic diameter (as measured) from time of operation to slaughter. Figs. 19*B* and 20*B* show that most of the fresh inferior vena caval autografts were larger than the aorta at slaughter while most of the delayed vena caval autografts were smaller. In

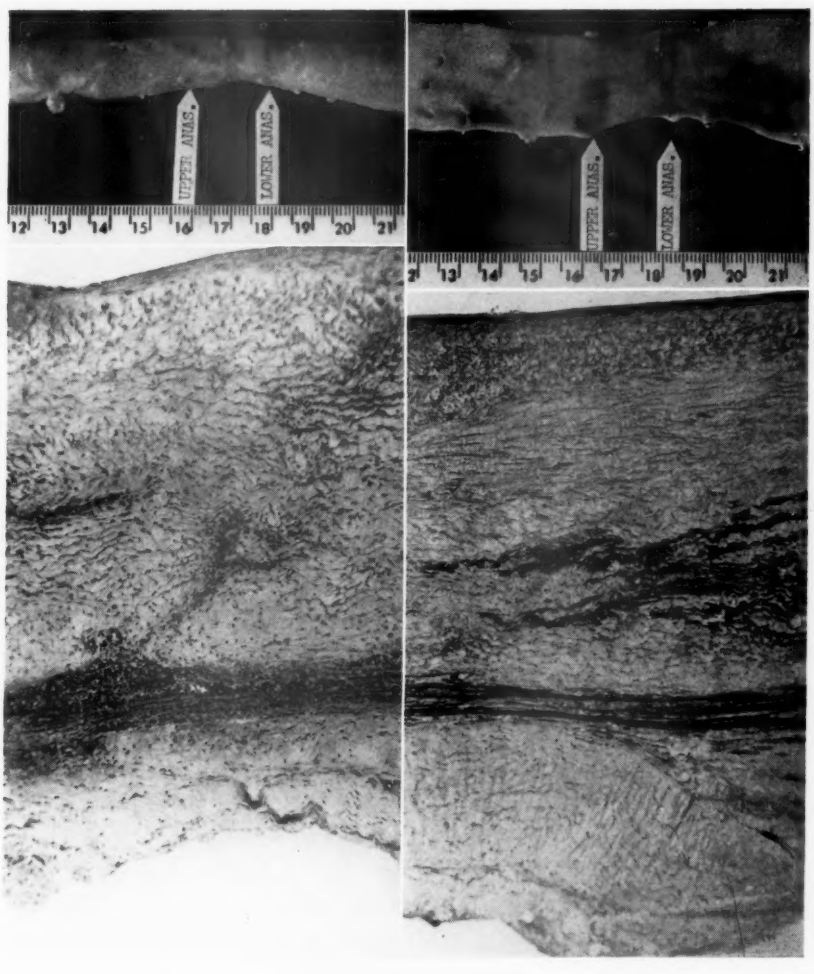


Fig. 10*B* (Pig 146 [21]).—This is the same graft as shown in Fig. 10*A*, but after being in place in a nonlitter mate for 170 days with a 562 per cent increase in pig weight. The upper anastomosis was performed with continuous 00000 catgut using the Carrel method, and the lower anastomosis in the same manner with 00000 silk. Dimensional changes were: (1) (crown-rump length, 67 per cent increase, (2) graft length, 100 per cent increase, (3) graft diameter, 80 per cent increase, (4) diameter of upper anastomosis, 140 per cent increase. (5) diameter of lower anastomosis, 100 per cent increase, (6) distance from graft to left renal artery, 62 per cent increase, (7) diameter of aorta 1 cm. above graft, 108 per cent increase, (8) diameter of aorta 4 cm. below graft, 146 per cent increase.

a, There is no significant constriction of the graft.

b, The inner surface is smooth and glistening. The dark staining of the graft and distal aorta is due to the pig's not being completely bled out at slaughter.

c, The wall is composed of heavy connective tissue lined internally by endothelium.

d, There is little elastic tissue remaining in the wall. This graft classifies as partially satisfactory.

this respect, the delayed inferior vena caval autografts resembled aortic homografts.

As shown in Fig. 21*A*, preservation did not appear to alter the growth changes of inferior vena caval homografts. Also, the type of preservative

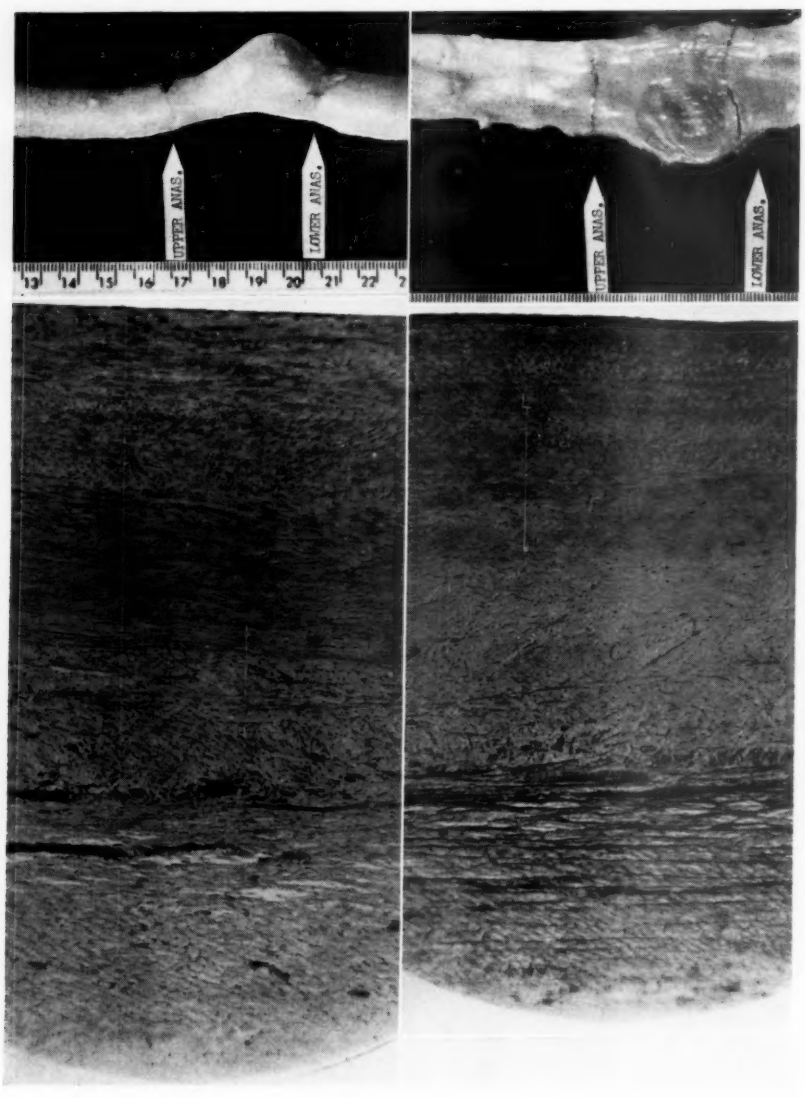


Fig. 11 (Pig 149 [14]).—This fresh inferior vena caval autograft has been in place for 245 days with a pig weight increase of 1,128 per cent. Both anastomoses were performed with continuous 00000 silk using the Carrel method. Dimensional changes were: (1) crown-rump length, 112 per cent increase, (2) graft length, 137 per cent increase, (3) graft radius, 328 per cent increase, (4) radius of upper anastomosis, 108 per cent increase, (5) radius of lower anastomosis, 173 per cent increase, (6) distance from graft to right renal artery, 77 per cent increase, (7) radius of aorta 2 cm. above graft, 257 per cent increase, (8) radius of aorta 2 cm. below graft, 357 per cent increase.

***a*, There is definite dilatation of this graft in an anterior direction.**

***b*, The surface of the graft is smooth and glistening. The wall is thicker than the aorta except in the area of dilatation where it is thinner.**

***c*, The wall is composed of heavy connective tissue lined internally by endothelium.**

***d*, Some elastic tissue is present in the outer portion of the wall. This graft classifies as unsatisfactory on the bases of dilatation.**

medium (light mineral oil, Ringer's solution, or Tyrode's solution) did not appear to significantly effect these changes. These grafts tended to remain stationary or actually to decrease in size from time of operation to slaughter. As a consequence of this tendency (Fig. 21*B*), these grafts, though larger than the aorta at implantation, were all smaller at time of slaughter.

In Fig. 22*A*, the averages of the dimensional changes of the different types of grafts are shown. The only grafts which increased at essentially the same

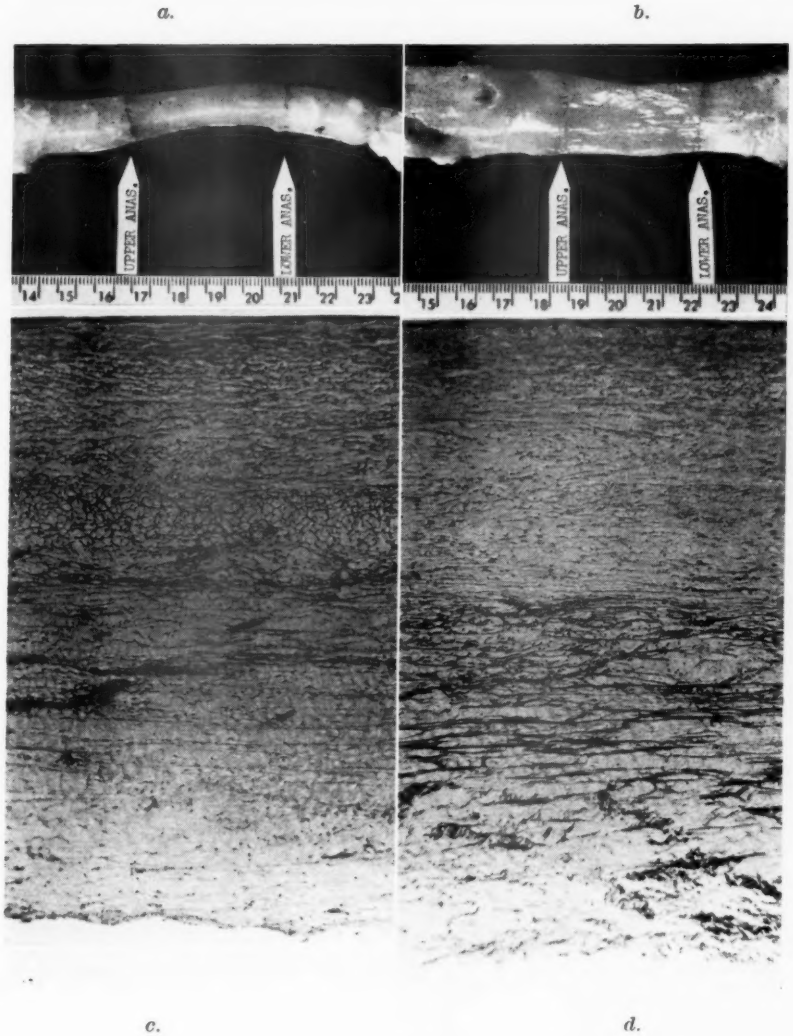


Fig. 12 (Pig 133 [8]).—This fresh inferior vena caval autograft has been in place for 265 days with a pig weight increase of 947 per cent. Both anastomoses were performed with continuous 00000 silk using the Carrel method. Dimensional changes were: (1) crown-rump length, 99 per cent increase, (2) graft length, 211 per cent increase, (3) graft radius, 19 per cent increase, (4) radius of upper anastomosis, 100 per cent increase, (5) radius of lower anastomosis, 69 per cent increase, (6) distance from graft to right renal artery, 85 per cent increase, (7) radius of aorta 1 cm. above graft, 150 per cent increase, (8) radius of aorta 2 cm. below graft, 167 per cent increase.

a, Differing from the graft shown in Fig. 11, this graft is slightly smaller than the aorta.

b, The inner surface is smooth and velvety.

c, The wall is composed of heavy connective tissue lined internally by endothelium.

d, Some elastic tissue is present in the outer portion of the graft wall. This graft classifies as partially satisfactory.

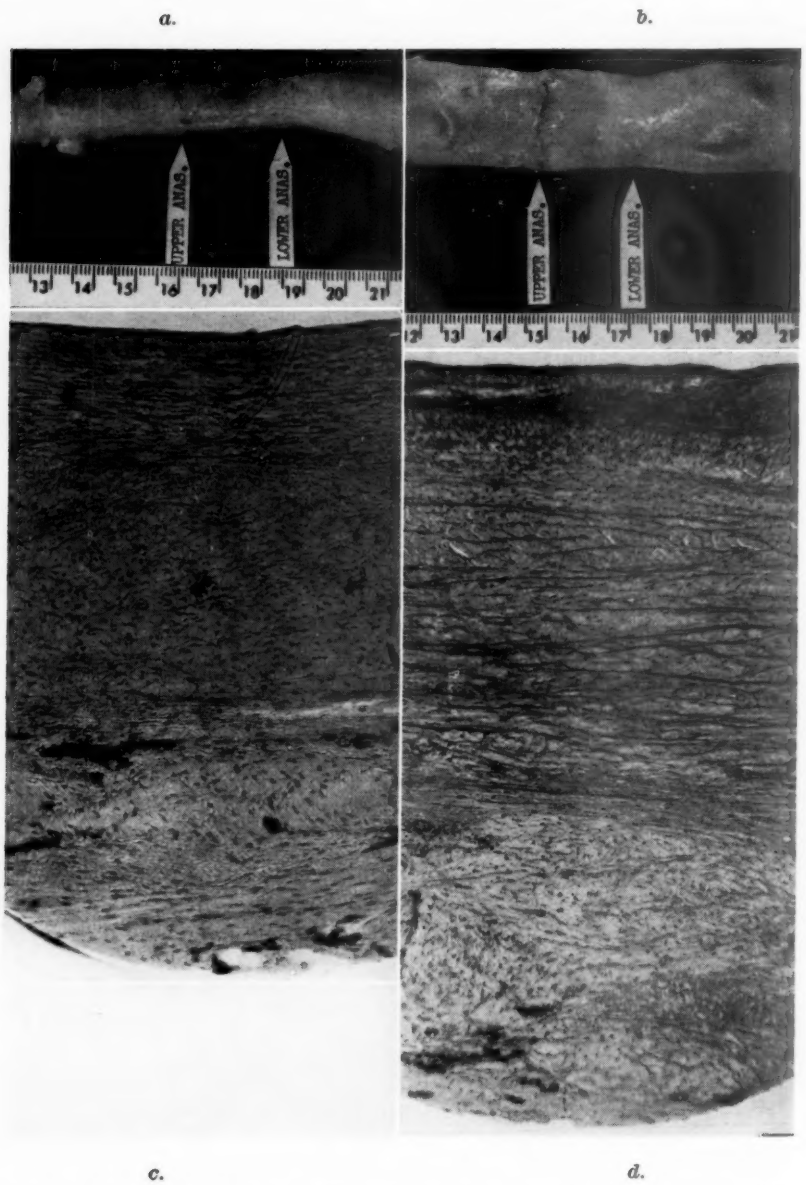


Fig. 13 (Pig 90 [67]).—This inferior vena caval autograft, previously stored 24 days in Tyrode's solution, has been in place for 257 days with a pig weight increase of 865 per cent. The upper anastomosis was performed with continuous 00000 silk using the Carrel method, and the lower anastomosis in the same manner with 00000 catgut. Dimensional changes were: (1) crown-rump length, 90 per cent increase, (2) graft length, 13 per cent increase, (3) graft radius, 33 per cent increase, (4) radius of upper anastomosis, 69 per cent increase, (5) radius of lower anastomosis, 62 per cent increase, (6) distance from graft to left renal artery, 115 per cent increase, (7) radius of aorta 2 cm. above graft, 150 per cent increase, (8) radius of aorta 3 cm. below graft, 190 per cent increase.

a, The graft is slightly smaller than the aorta.

b, The inner surface is smooth and even.

c, The wall is composed of heavy connective tissue lined internally by endothelium.

d, Elastic tissue is present in the middle portion of the graft wall. This graft classifies as partially satisfactory.

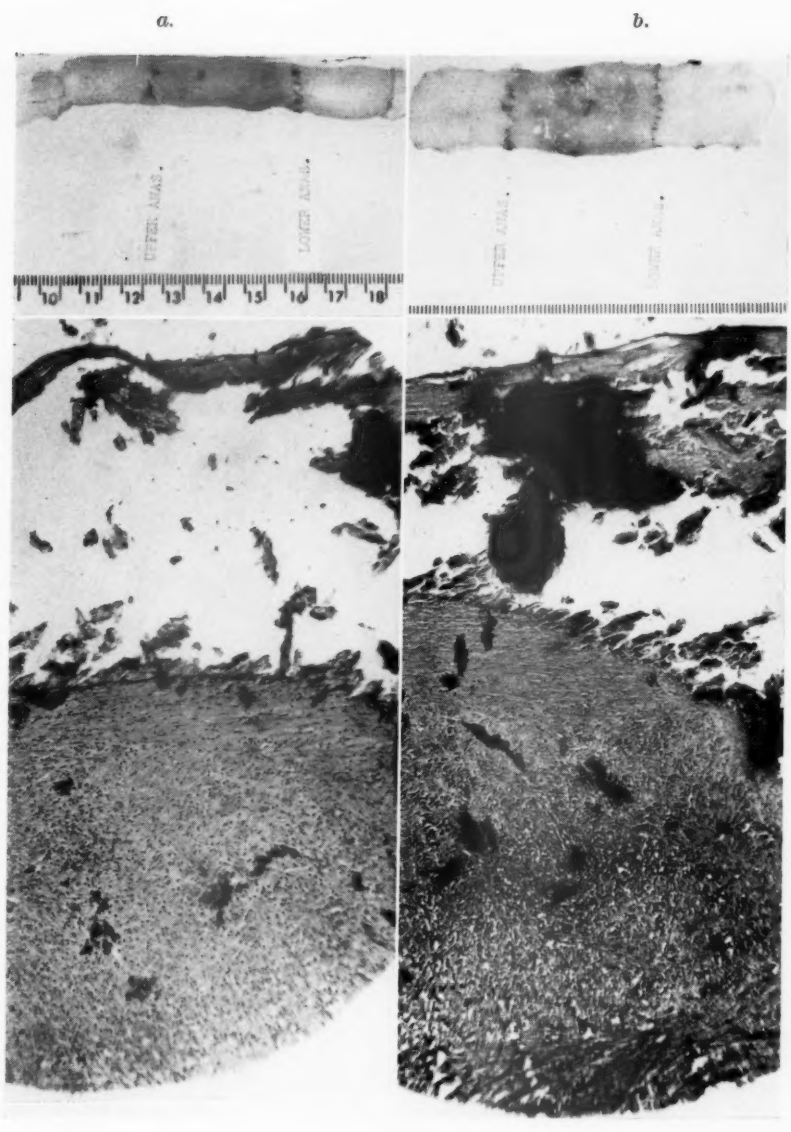


Fig. 14 (Pig 35 [20]).—This fresh inferior vena caval homograft implanted in the abdominal aorta of a litter mate pig has been placed for 168 days with a pig weight increase of 483 per cent. Both anastomoses were performed with continuous 00000 silk using the Carrel method. Dimensional changes were: (1) graft length, 90 per cent increase, (2) graft diameter, 71 per cent increase, (3) diameter of upper anastomosis, 83 per cent increase, (4) diameter of lower anastomosis, 67 per cent increase, (5) diameter of aorta 2 cm. above graft, 109 per cent increase, (6) diameter of aorta 2 cm. below graft, 150 per cent increase.

a, The graft is approximately the same caliber as the aorta. However, it differs from the aorta in that it is inelastic, and in the middle section its walls are brittle and cannot be compressed without cracking.

b, Yellow brittle plaques lie close beneath the inner surface in the middle portion of the graft.

c, Degenerative changes are seen in the inner half of the wall.

d, No elastic tissue is seen in this section. This graft classifies as unsatisfactory on the basis of degenerative change (calcification).

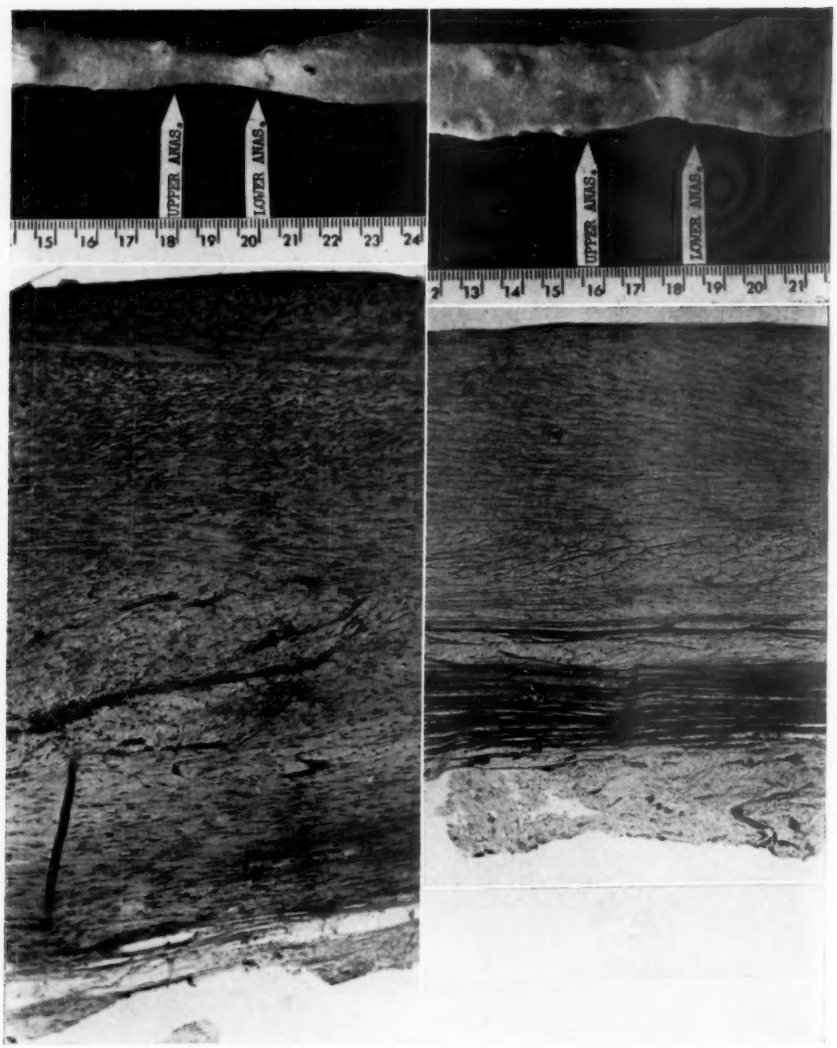


Fig. 15 (Pig 107 [83]).—This inferior vena caval homograft, previously stored 54 days in light mineral oil, has been in place in a nonlitter mate for 232 days with a pig weight increase of 853 per cent. The upper anastomosis was performed with continuous 00000 catgut using the Carrel method, and the lower anastomosis in the same manner with 00000 silk. Dimensional changes were: (1) crown-rump length, 87 per cent increase, (2) graft length, 26 per cent increase, (3) graft diameter, 0 per cent increase, (4) diameter of upper anastomosis, 69 per cent increase, (5) diameter of lower anastomosis, 62 per cent increase, (6) distance from graft to left renal artery, 89 per cent increase, (7) diameter of aorta 2 cm. above graft, 118 per cent increase, (8) diameter of aorta 3 cm. below graft, 228 per cent increase.

a, There is definite constriction of the lower third of the graft. Dilatation is present distally.

b, The wall in the narrowed area is composed of tough heavy tissue which appears to be drawing the surrounding tissues in toward it.

c, The wall consists of dense connective tissue.

d, Considerable elastic tissue is present in the outer portion of the graft wall. This graft classifies as unsatisfactory on the basis of stenosis.

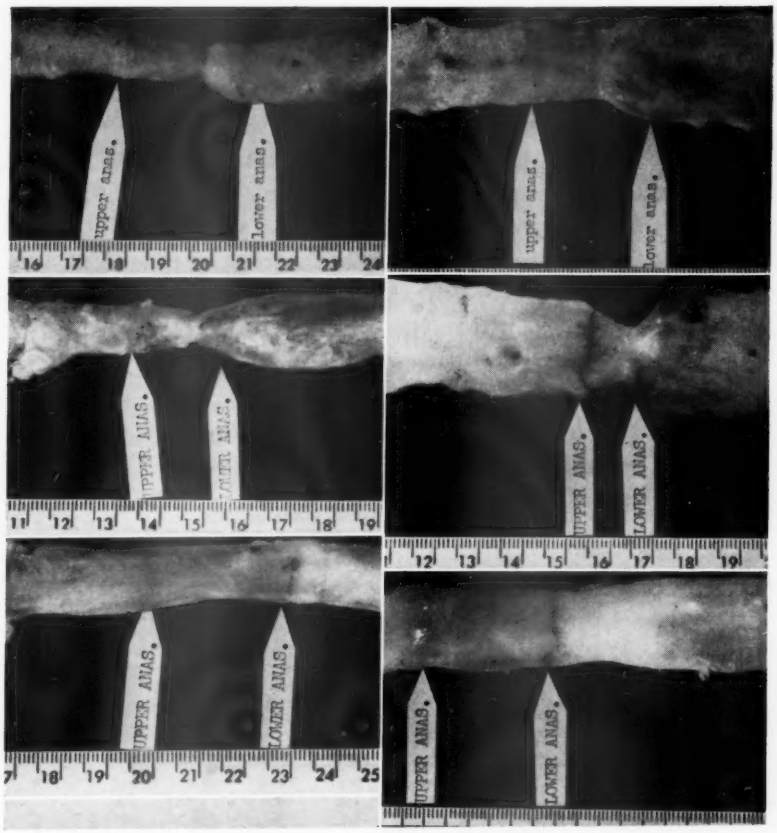


Fig. 16.—Three different inferior vena caval homografts are shown in this composite figure.

In *a* and *b*, a fresh inferior vena caval homograft which has been in place in a nonlitter mate (Pig 87 [65]) for 188 days is shown. The pig weight increase was 777 per cent. Both anastomoses were performed with continuous 00000 catgut using the Carrel method. Dimensional changes were: (1) graft length, 132 per cent increase, (2) graft diameter, 14 per cent decrease, (3) diameter of upper anastomosis, 82 per cent increase, (4) diameter of lower anastomosis, 155 per cent increase, (5) distance from graft to right renal artery, 114 per cent increase, (6) diameter of aorta 2 cm. above graft, 120 per cent increase, (7) diameter of aorta 2 cm. below graft, 220 per cent increase. Note the constriction in the lower portion of the graft wth dilatation distally. This graft classifies as unsatisfactory on the basis of stenosis.

a^1 and b^1 show an inferior vena caval homograft, previously stored 102 days in Tyrode's solution, which has been in place in a nonlitter mate (Pig 118 [94]) for 169 days with a pig weight increase of 466 per cent. The upper anastomosis was performed with continuous 00000 silk using the Carrel method, and the lower anastomosis in the same manner with 00000 catgut. Dimensional changes were: (1) crown-rump length, 69 per cent increase, (2) graft length, 8 per cent decrease, (3) graft diameter, 41 per cent decrease, (4) diameter of upper anastomosis, 58 per cent increase, (5) diameter of lower anastomosis, 33 per cent increase, (6) distance from graft to left renal artery, 77 per cent increase, (7) diameter of aorta 2 cm. above graft, 83 per cent increase, (8) diameter of aorta 2 cm. below graft, 183 per cent increase. There is marked constriction of the distal one-third of the graft with poststenotic dilatation. At the time of slaughter, many collateral arterial channels were present about the graft. This graft classifies as unsatisfactory on the basis of stenosis.

a^2 and b^2 show an inferior vena caval homograft, previously stored 105 days in Ringer's solution, which has been in place in a nonlitter mate (Pig 106 [82]) for 183 days with a pig weight increase of 652 per cent. The upper anastomosis was performed with continuous 00000 catgut using the Carrel method, and the lower anastomosis in the same manner with 00000 silk. Dimensional changes were: (1) crown-rump length, 82 per cent increase, (2) graft length, 71 per cent increase, (3) graft diameter, 19 per cent increase, (4) diameter of upper annastomosis, 100 per cent increase, (5) diameter of lower anastomosis, 67 per cent increase, (6) distance from graft to left renal artery, 173 per cent increase, (7) diameter of aorta 2 cm. above graft, 160 per cent increase, (8) diameter of aorta 3 cm. below graft, 170 per cent increase. There is no significant constriction. This graft classifies as partially satisfactory.

rate as the aorta were the fresh aortic autografts. The aortic homografts, fresh or preserved, increased at a slower rate than the aorta. The inferior vena caval homografts, fresh or preserved, on an average decreased in diameter from time of operation to slaughter. Fresh inferior vena caval autografts had an average increase slightly greater than the aorta (but the individual experiments varied greatly among themselves), while the delayed grafts resembled the aortic homografts in their dimensional changes. In Fig. 22*B*, it is seen that, because of the growth tendencies of the various types of grafts, (1) the aortic autografts were the only grafts which maintained the same size relationship to the aorta with growth that was present at implantation, (2) because of dilatation of some fresh inferior vena caval autografts (Fig. 11) the graft-aortic radius ratio increased moderately from operation to slaughter, and (3) because of the tendency of the other types of grafts not to increase as rapidly as the aorta, the graft-aortic caliber ratio decreased from time of operation to slaughter. This was most pronounced in the case of the inferior vena caval homografts.

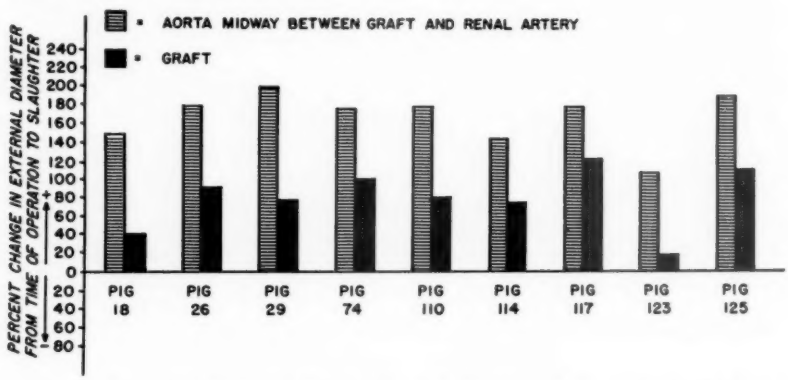


Fig. 17*A*.—Fresh aortic homografts implanted in the abdominal aortas of young pigs. Per cent change in external diameter from time of operation to slaughter. The crosshatched columns represent the change in the diameter of the aorta midway between graft and renal artery, while the solid columns represent that in the diameter of the graft. All grafts increased in external diameter from time of operation to slaughter but at a slower rate than did the aorta of the host.

STENOSIS

All of the grafts showing stenosis had the greatest constriction toward their mid-portion. The growth changes at the anastomoses generally followed those of the aorta rather closely.

As shown in Table IV, of the 76 grafts open at time of slaughter whose dimensions were not appreciably influenced by the method of suture, there were 15 instances of stenosis. No fresh aortic or inferior vena caval autograft was stenosed. One delayed inferior vena caval autograft preserved 14 days in Tyrode's solution prior to implantation was stenosed at time of slaughter. Three of 9 fresh aortic homografts were stenosed (Fig. 4). Three of 32 delayed aortic homografts were stenosed. Two of 3 fresh inferior vena caval homografts were stenosed (Fig. 16). Six of 11 delayed inferior vena caval homografts (Figs. 15 and 16) were stenosed. No relationship was observed between the duration of the period of preservation of aortic or inferior vena

caval homografts prior to implantation and the development of stenosis in these grafts after implantation. The 3 inferior vena caval homografts shown in Fig. 16 illustrate this point. Of these grafts 2 became stenosed, 1 a fresh and 1 a delayed inferior vena caval homograft preserved for 102 days in Tyrode's solution prior to implantation, while stenosis did not occur in a delayed inferior vena caval homograft preserved for 105 days in Ringer's solution prior to implantation.

DILATATION

As shown in Table IV, dilatation did not occur in any of 55 aortic or inferior vena caval homografts or in any of 6 fresh aortic autografts open at the time of slaughter. However, 3 of 7 inferior vena caval autografts were dilated in the fresh group (Fig. 11) and 1 of 8 in the delayed group. Dilatation in these grafts was of an asymmetrical type involving the anterior walls of the grafts predominantly.

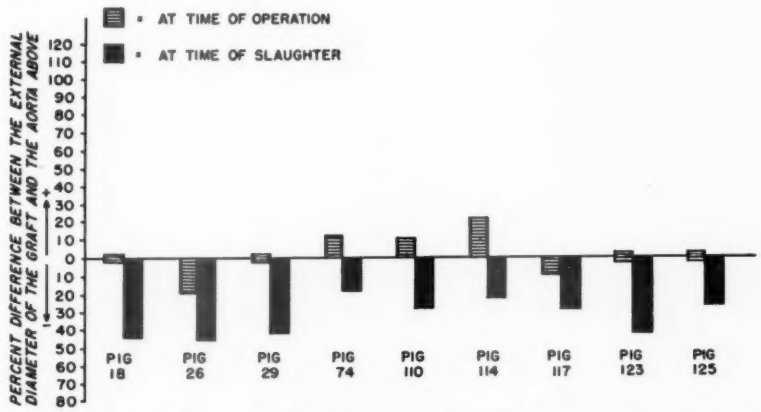


Fig. 17*B*.—Fresh aortic homografts implanted in the abdominal aortas of young pigs. Per cent difference between the external diameter of the graft and the aorta midway between graft and renal artery. The crosshatched columns represent the difference at the time of operation, while the solid columns represent that at the time of slaughter. Columns below the zero line indicate that the graft is smaller than the aorta midway between graft and renal artery, above the line that the graft is larger. As a consequence of their reduced rate of growth as compared to the aortas (Fig 17*A*), these grafts were all smaller than the aortas at slaughter.

ANASTOMOTIC GROWTH

The 168 anastomoses (84 grafts), patent at the time of slaughter of the pigs, included the following types: (A) 105 anastomoses performed with continuous silk (00000 in 95 instances, 0000 in 8, and 000000 in 2) using the end-on coaptation method, (B) 43 anastomoses performed with continuous catgut (00000 in 41 and 0000 in 2) using the end-on coaptation method, (C) 10 anastomoses performed with continuous 00000 silk using the everting mattress method, (D) 5 anastomoses performed with continuous 00000 catgut using the everting mattress method, (E) 3 anastomoses performed with 00000 silk using a continuous everting mattress suture posteriorly and interrupted stitches of the same type anteriorly, and (F) 2 anastomoses performed with 00000 silk using a continuous end-on type suture posteriorly and interrupted stitches of the same type anteriorly. From the technical standpoint, catgut and silk were equally satis-

factory. In no instance did a size 00000 catgut or silk suture break during the performance of an anastomosis.

At the time of slaughter, the continuous silk sutures were intact in all instances except one. In this, the lower aortic-graft anastomosis of an inferior vena caval autograft, the continuous 000000 silk suture employed as an over-and-over stitch had broken. By the time of slaughter, the catgut suture had been completely absorbed in all instances. Anastomotic constriction was observed only in those anastomoses performed with continuous silk sutures. Constriction was present in each of 10 anastomoses performed with 00000 silk by the everting mattress technique. However, in only 3 of 105 anastomoses (Fig. 9) performed by the end-on coaptation method using a continuous silk suture was constriction present at the time of slaughter. Constriction was not present in any of the anastomoses performed with continuous catgut or in any of the anastomoses performed with silk in which the anterior row was placed interrupted (Fig. 2).

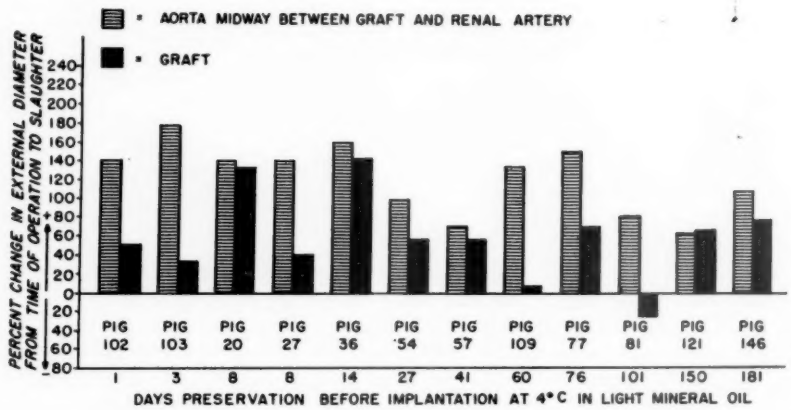


Fig. 18A.—Delayed aortic homografts in light mineral oil implanted in the abdominal aortas of young pigs. Per cent change in external diameter from time of operation to slaughter. The crosshatched columns represent the change in the diameter of the aorta midway between graft and renal artery, while the solid columns represent that in the diameter of the graft. With two exceptions, these grafts all increased in external diameter from time of operation to slaughter but at a slower rate than did the aortas. The graft preserved for 101 days prior to implantation decreased 22 per cent in external diameter from time of operation to slaughter. However, this graft was 50 per cent larger than the aorta at implantation. The graft preserved for 150 days (segment of same donor vessel as graft preserved for 101 days) increased at a slightly greater rate than did the aorta. No definite relationship was observed between the duration of the period of preservation and the changes in the external diameters of these grafts.

It is difficult to compare the extent of anastomotic growth obtained in different pigs by various techniques. Because the caliber change of the graft influences that of the lower anastomosis, it is not possible to compare accurately the external diameter change of the lower anastomosis performed by various techniques. A more accurate comparison can be made between the growth changes of the upper anastomosis. Forty-nine upper aortic-graft anastomoses performed with continuous silk using the end-on coaptation type of approximation showed no evidence of constriction. These anastomoses increased an average of 94 per cent in external diameter from time of operation to slaughter. Twenty-three upper aortic-graft anastomoses performed with continuous 00000 catgut placed

in the same way increased an average of 106 per cent from time of operation to slaughter.

DISCUSSION

Some important aspects of vascular grafts will be considered under the following headings:

A. Histologic Survival of Vascular Grafts Implanted in the Arterial System.—

Fresh arterial autografts: Without exception of note, previous experiments by others have indicated that arterial autografts of the arterial system maintain their cellular integrity and resemble the recipient artery in all obvious respects. This has likewise been our finding (Fig. 2). Such observations indicate that the operative interruption of the vasa vasorum of the graft does not seriously impair its nutrition. It is probable that direct absorption from the blood stream and surrounding tissue fluids at least maintains the minimal requirements of the graft cells until revascularization of the graft occurs from the arterial ends and adjacent areolar tissue.

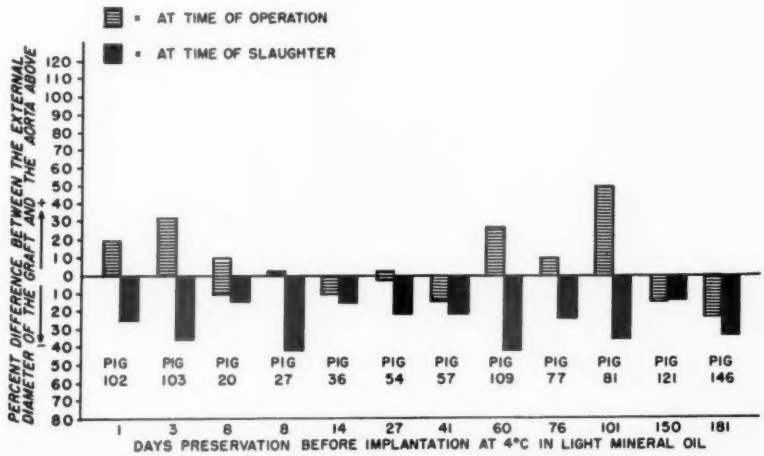


Fig. 18*B*.—Delayed aortic homografts in light mineral oil implanted in the abdominal aortas of young pigs. Per cent difference between the external diameter of the graft and the aorta midway between graft and renal artery. The crosshatched columns represent the difference at the time of operation, while the solid columns represent that at the time of slaughter. Columns below the zero line indicate that the graft is smaller, above the line that the graft is larger. As a consequence of their reduced rate of growth as compared to the aortas (one exception—Pig 121, Fig. 18*A*), these grafts were all smaller than the aortas at slaughter.

Fresh venous autografts: Klotz, Permar, and Guthrie (1923) stated that a segment of vein engrafted on an artery shows thickening of the wall through fibrosis with disappearance of the muscular tissue. Others, including Johnson, Kirby, Griefenstein, and Castillo (1949) and Shumacker, Schloss, Freeman, Wayson, and Stahl (1950), observed thickening of the wall due to fibrosis but without the disappearance of the muscular tissue. However, they did not observe hypertrophy of the muscular elements. It is commonly held, as recently stated by Humphreys (1952), that "a vein is capable of extraordinary hypertrophy of both muscular and fibrous tissue if called upon (as when used for a graft) to serve as an artery." In our studies of 7 fresh inferior vena caval

autografts implanted in the abdominal aorta of the growing pig that were open at the time of slaughter, an average of 225 days later, we found the wall to be composed of dense connective tissue lined internally by endothelium (Figs. 11 and 12). Smooth muscle cells, if present, could not be identified. The fresh venous autograft in the arterial system, differing from the fresh arterial autograft, changes greatly. Whether this adaptation of the graft to its environment is brought about by its own cells, by replacement, or by reinforcement from the surrounding tissues is not certain.

Delayed venous autografts: We are not aware of previous histologic studies of delayed venous autografts implanted in the arterial system. We observed these grafts at time of slaughter of the pigs, as with the fresh venous autografts, to be composed of dense connective tissue lined internally by endothelium (Fig. 13).

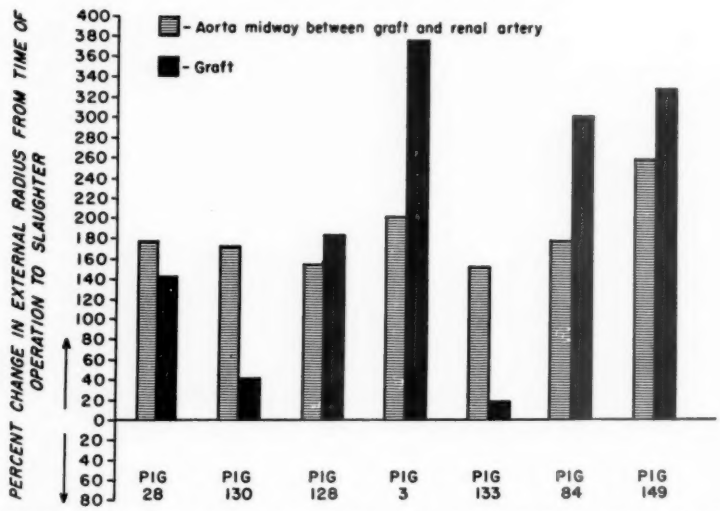


Fig. 19*A*.—Fresh inferior vena caval autografts implanted in the abdominal aortas of young pigs. Per cent change in external radius from time of operation to slaughter. The crosshatched columns represent the change in the radius of the aorta midway between graft and renal artery, while the solid columns represent that in the radius of the graft. Three grafts increased at a rate considerably faster than the aorta, 2 at about the same rate, and 2 at a rate considerably slower than the aorta.

Arterial homografts: Miller, Callow, Welch, and MacMahon (1951) observed arterial homografts, both fresh and preserved (the latter up to as long as 22 days in Tyrode's solution prior to implantation), to undergo a necrosis of all layers with replacement by the host. Swan (1952) stated that "all cellular elements in the graft are destroyed by host reaction by the end of the third week; the elastic tissue of the media, however, persists for a period of at least 2 years." In our studies, we have observed both fresh and delayed aortic homografts, the latter preserved up to as long as 181 days prior to implantation, to have similar histologic fates (Figs. 4 and 10*B*). These grafts become connective tissue tubes lined internally by endothelium in which the elastic tissue of the original graft persists for prolonged periods. In only one instance (Fig. 3) was cellular integrity preserved. This occurred in an aortic homograft preserved one day in Tyrode's solution prior to implantation in the abdominal aorta

of a nonlitter mate pig. It seems odd that this occurred in a nonlitter mate pig while each of 5 fresh abdominal aortic homografts transplanted into litter mate pigs lost its cellular integrity and was replaced with connective tissue by the host.

Venous homografts: At the time of slaughter of the pigs, this type of graft, fresh or preserved, was lined internally by endothelium and its wall, similar to the venous autograft, was composed of fibroblasts, many collagen fibers, and some elastic fibers. Because of the uncertainty regarding preservation of cellular integrity in venous autografts, it is difficult to be more certain about venous homografts when their histologic appearance at the time of slaughter is very similar to that of the venous autografts. However, in view of the loss of cellular integrity of arterial homografts, it seems logical to assume that complete replacement by the host also occurs in the case of venous homografts.

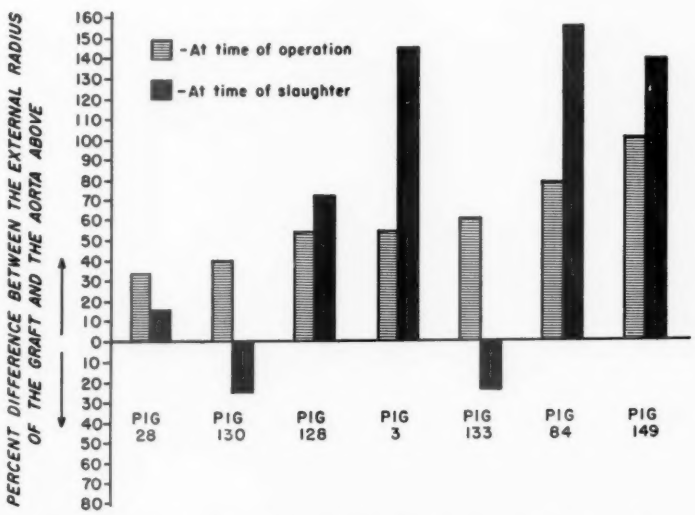


Fig. 19*B*.—Fresh inferior vena caval autografts implanted in the abdominal aortas of young pigs. Per cent difference between the external radius of the graft and the aorta midway between graft and renal artery. The crosshatched columns represent the difference at the time of operation, while the solid columns represent that at the time of slaughter. Columns below the zero line indicate that the radius of the graft is smaller than that of the aorta midway between graft and renal artery, above the line that the radius of the graft is larger. All grafts were larger than the aorta at implantation, but because of their variable radius changes (Fig. 19*A*), some got still larger and others got smaller relative to the aortic radius.

B. Histologic Fates and Dimensional Changes.—In view of the marked histologic difference between the implanted graft and the aorta (Figs. 4 to 15), except in the case of the fresh arterial autograft (Fig. 2), it would be surprising if the dimensional changes of these histologically dissimilar grafts were identical with those of the aortas. It seems entirely reasonable to assume that any blood vessel replacement that is distinguishable from the normal vessel can never be a truly satisfactory substitute for that vessel (Table III). In this regard, nature cannot be improved upon. Her design is the best. Thus, one would expect fresh arterial autografts to grow at a rate comparable to the normal artery. This is what they do (Fig. 22*A*). Such has also been shown by Johnson, Kirby, Allam, and Hagan (1951) and Everson and Southwick (1951).

The fibrous character of the wall of the arterial homograft, fresh or preserved, would lead one to suspect that these grafts would lag behind the normal artery in their growth. Our observations (Figs. 17*A*, 17*B*, 18*A*, 18*B*, 22*A* and 22*B*) indicate that this occurs with regularity. Johnson, Kirby, Allam, and Hagan (1951), on the basis of 2 fresh aortic homografts implanted in the abdominal aortas of pigs that were open at slaughter, concluded that the graft grew at the same rate as the aorta. However, Johnson, Kirby, and Horn (1952) observed 6 of 7 aortic homografts preserved from 5 to 28 days prior to implantation to lag behind the aorta in most instances. We would say on the basis of more observations (41), that fresh and preserved aortic homografts both lag behind the aorta in diameter changes and both to about the same degree.

The variability in the radius changes of the fresh venous autografts is puzzling (Figs. 19*A* and 19*B*). Could it be that the surrounding tissues, for reasons as yet obscure, in certain instances react quicker and to a greater degree to reinforce and nourish the graft?

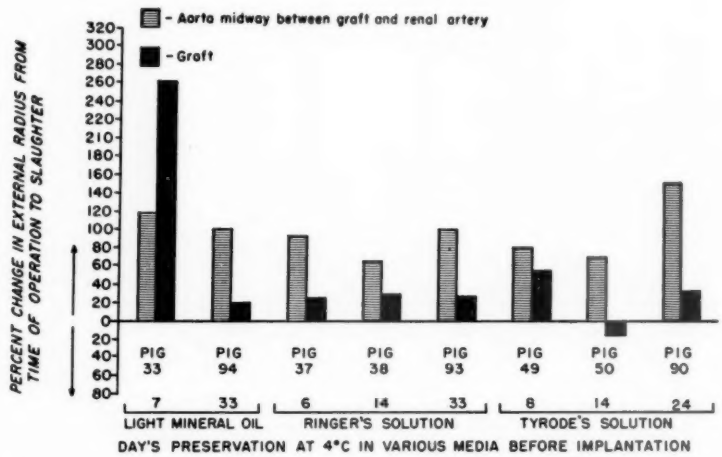


Fig. 20*A*.—Delayed inferior vena caval autografts implanted in the abdominal aortas of young pigs. Per cent change in external radius from time of operation to slaughter. The crosshatched columns represent the change in the radius of the aorta midway between graft and renal artery, while the solid columns represent that in the radius of the graft. One graft increased at a rate faster than the aorta, 6 increased at a slower rate, and 1 actually decreased in radius from time of operation to slaughter.

Preservation appeared to alter the dimensional changes of the venous autografts (Figs. 19*A* to 20*B*). This evidence is not conclusive, but it is suggestive. If such be a valid observation, it could be that preservation altered the graft tissue so that the response of the body to it was different than to the fresh fully viable autogenous venous tissue. The delayed inferior vena caval autografts, in the main, resembled aortic homografts in their dimensional changes (Fig. 22*A*).

A further enigma is the great difference between the caliber changes of the fresh venous autografts and venous homografts, fresh or delayed (Figs. 21*A* and 21*B*). While histologically similar at slaughter, the growth changes were in opposite directions, i.e., the fresh venous autografts got larger and the homografts got smaller. It is interesting to conjecture whether the connective tissue response of the body was more violent (constrictive) in the case of the foreign

(homologous) tissue than it was in the case of the native (autogenous) tissue. Also, whether our histologic appraisal of the situation at the time of slaughter was an accurate means of noting the difference, if such were present. Why stenosis should be a more frequent occurrence with venous than with arterial homografts is not clear from the histologic findings.

C. Histologic Fates and Degenerative Changes.—The loss of cellular integrity of a vascular homograft is a normal occurrence. However, the development of atheromatous or calcific (degenerative) changes in the "replaced" graft is an abnormal occurrence. A fresh arterial autograft probably does not have a greater tendency to develop degenerative changes than does the rest of the arterial system of that particular experimental animal or patient. On the other hand, a vascular homograft appears to have a much greater tendency to develop degenerative changes than does the arterial system into which it is implanted. This appears to be particularly true of formalin-fixed grafts (Peirce, Rheinlander, Moritz, Gross, and Merrill, 1949).

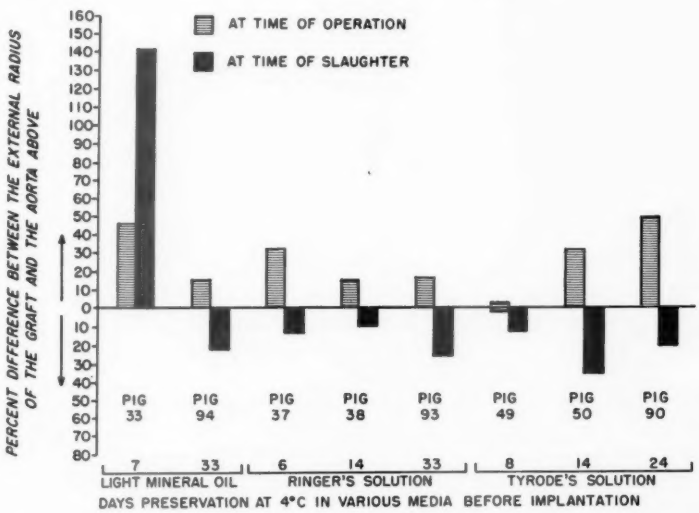


Fig. 20*B*.—Delayed inferior vena caval autografts implanted in the abdominal aortas of young pigs. Per cent difference between the external radius of the graft and the aorta midway between graft and renal artery. The crosshatched columns represent the difference at the time of operation, while the solid columns represent that at the time of slaughter. Columns below the zero line indicate that the radius of the graft is smaller than that of the aorta midway between graft and renal artery, above the line that the radius of the graft is larger. As a consequence of the reduced rate of growth of 7 of 8 of these grafts as compared to the aorta (Fig. 20*A*), these grafts, the same size or larger than the aorta at implantation, were all smaller at time of slaughter. Only 1 graft increased in radius relative to the aorta.

The degenerative changes that we have observed (Figs. 6 and 14) have been located about the remnants of the original grafts, i.e., elastic tissue elements. It seems probable that the ease of absorption of the homografted tissue by the host varies from graft to graft and from host to host.

We have observed no correlation between the age of the graft and the development of degenerative changes. Only 1 of 14 inferior vena caval homografts (including 11 delayed grafts preserved from 16 to 105 days) showed degenerative changes at the time of slaughter. This one instance occurred in a fresh graft implanted in a litter mate pig (Fig. 14). Two of 41 aortic

homografts (including 32 delayed grafts preserved from 1 to 181 days) showed degenerative change. Both instances occurred in delayed grafts, 1 preserved for 101 days in light mineral oil and the other preserved for 126 days in Ringer's solution. The graft showing degenerative change that had been stored for 101 days gave valuable information because 2 other segments of the same donor artery preserved in the same bottle of light mineral oil for 150 and 181 days were used as grafts (Figs. 6, 9, 10*A*, and 10*B*) and showed no degenerative change. An important question, but one which cannot be answered from our data, is whether this degenerative change would also have occurred if a fresh segment of this same vessel had been implanted in the arterial system of that particular pig. These degenerative changes appear to be the result of a specific host-graft reaction which, in our experience, is but little related to the

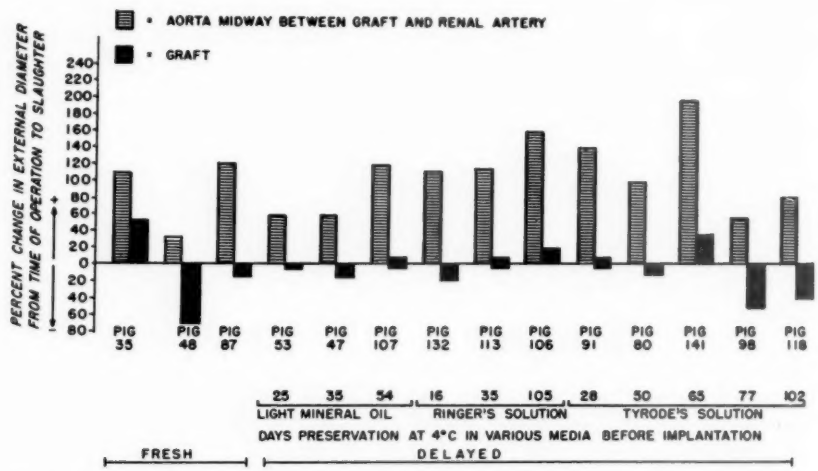


Fig. 21*A*.—Inferior vena caval homografts implanted in the abdominal aortas of young pigs. Per cent change in external diameter from time of operation to slaughter. The cross-hatched columns represent the change in the diameter of the aorta midway between graft and renal artery, while solid columns represent that in the diameter of the graft. These grafts, fresh or preserved, exhibited a pronounced tendency to stay stationary or actually to decrease in diameter from time of operation to slaughter. No definite relationship was observed between the duration of the period of preservation and the changes in the external diameters of the delayed grafts.

age of the graft at implantation (Sauvage and Harkins, 1952). However, it seems probable that after sufficiently long periods of preservation alterations would occur in the graft tissues which *would* render them more liable to the development of degenerative changes than would be the case if they had been preserved for shorter periods. If such alterations do finally occur with preservation, it would be of importance to know how long grafts might be kept before they occur. Unfortunately, our data do not provide information in this regard other than that, for the types of grafts studied, the periods of preservation evaluated (up to 181 days in the case of arterial homografts and up to 105 days in the case of venous homografts) were not necessarily associated with the development of degenerative changes in these grafts after implantation in the abdominal aorta of the growing pig.

The absence of degenerative change in the 15 inferior vena caval autografts (7 fresh and 8 delayed) that were open at the time of slaughter suggests that

these grafts may have a very low incidence of degenerative change. Murray (1952) reports that an external jugular vein graft which had functioned in the carotid artery of a dog for 9 years showed "some arteriosclerotic change at one point in the vessel and on section there is a small amount of bone formed at this area." It would seem that the host would be better able to handle autogenous tissue, even if nonviable, than it would homologous tissue.

D. Principles of Vascular Graft Preservation.—Except in very unusual circumstances when vascular homografts are to be employed, they must of necessity be delayed grafts preserved by one means or another. In general, grafts may be preserved at room temperature, at temperatures slightly above 0° C., or at temperatures below 0° C.

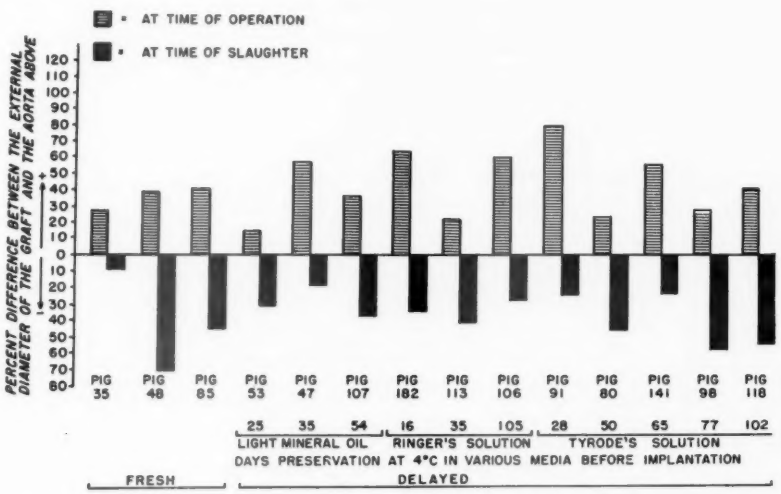

AT TIME OF OPERATION
AT TIME OF SLAUGHTER
PERCENT DIFFERENCE BETWEEN THE EXTERNAL DIAMETER OF THE GRAFT AND THE AORTA ABOVE
120 110 100 90 80 70 60 50 40 30 20 10 0 10 20 30 40 50 60 70 80
PIG 35
PIG 48
PIG 85
PIG 53
PIG 47
PIG 107
PIG 182
PIG 113
PIG 106
PIG 91
PIG 80
PIG 141
PIG 98
PIG 118
25 35 54 16 35 105 28 50 65 77 102
LIGHT MINERAL OIL
RINGER'S SOLUTION
TYRODE'S SOLUTION
DAYS PRESERVATION AT 4°C IN VARIOUS MEDIA BEFORE IMPLANTATION
FRESH
DELAYED

Fig. 21*B*.—Inferior vena caval homografts implanted in the abdominal aortas of young pigs. Per cent difference between the external diameter of the graft and the aorta midway between graft and renal artery. The crosshatched columns represent the difference at the time of operation, while the solid columns represent that at the time of slaughter. Columns below the zero line indicate that the graft is smaller than the aorta midway between graft and renal artery, above the line that the graft is larger. As a consequence of their reduced rate of growth as compared to the aorta (Fig. 21*A*), these grafts, though larger than the aorta at implantation, were all smaller at time of slaughter.

Briefly, grafts preserved at room temperature must either be fixed by tissue fixatives, as formalin (Levin and Larkin, 1907 and 1909; Guthrie, 1919; Peirce, Rheinlander, Moritz, Gross, and Merrill, 1949) and alcohol (Paolucci and Tosatti, 1950) or by desiccation (Marrangoni and Cecchini, 1951). The latter method involves rapid freezing as a first stage with subsequent quick dehydration in a high vacuum. The graft, thus lyophilized, may then be kept indefinitely at room temperature. Of these methods, formalin may be discarded because of the high incidence of calcific change occurring in the implanted grafts, alcohol needs further experimental use to allow a decision as to its merits, and the freeze-drying method also needs more experimental work but appears to have real promise on the basis of preliminary observations.

Grafts have been preserved at temperatures slightly above 0° C. in a variety of media including defibrinated blood, Vaseline, and confined humid air (Carrel, 1910); modified Tyrode's solution containing 10 per cent homol-

ogous serum (Gross, Bill, and Peirce, 1949); and in Ringer's solution containing 10 per cent homologous serum (Swan, Robertson, and Johnson, 1950). Both Tyrode's and Ringer's solutions containing 10 per cent homologous serum have proved to be satisfactory media in which to preserve vascular segments. Our experiments have again confirmed this fact. In addition, we have compared these presumed "nutrient media" with an inert medium, namely, light mineral oil.

The use of mineral oil as a preservative medium has precedent in the fields of bacteriology and botany. Ungermann (1918) first reported conserving cultures of bacteria in dilute sera by covering them with a layer of mineral oil. Morton and Pulaski (1938) concluded that the mineral oil method is a generally practical and advantageous method for maintaining viable bacterial cultures for long periods of time. Buell and Weston (1947) concluded that the mineral oil method for the conservation of fungi is both effective and simple. Although the mechanism of the action of the mineral oil is not fully understood, the evidence indicates that it acts at least by preventing dehydration of the cultures and slowing down metabolic activity and growth of the fungi. We do not propose that a complex tissue, such as a blood vessel, should react in the same way as unicellular organisms. However, it is interesting

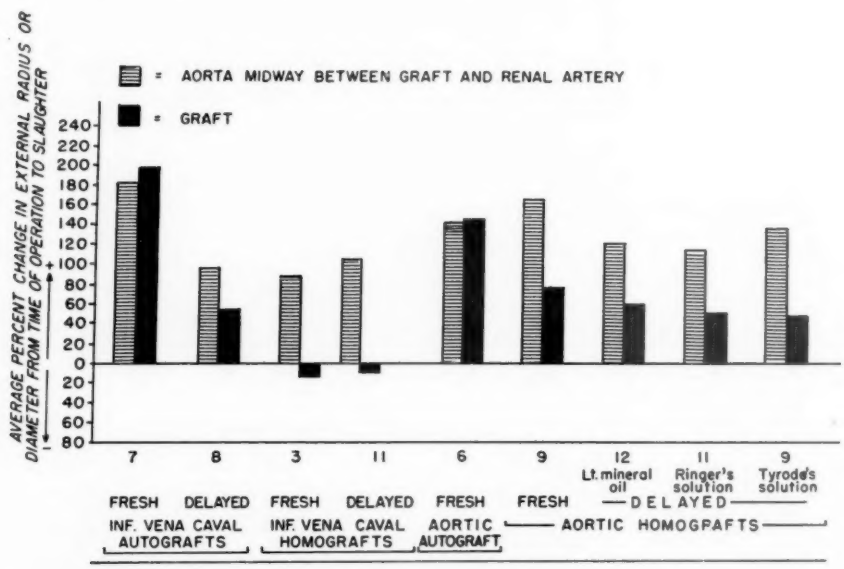


Fig. 22*A*.—Seventy-six vascular grafts implanted in the abdominal aortas of young pigs (open at slaughter). Average per cent change in external radius or diameter from time of operation to slaughter. Radius changes are averaged for the inferior vena caval autografts (both fresh and delayed), while diameter changes are averaged for the other types of grafts. The crosshatched columns represent the average change in the radius or diameter of the aortas midway between graft and renal artery, while the solid columns represent that in the radius or diameter of the grafts. It appears that preservation altered the radius changes of the inferior vena caval autografts but did not alter the diameter changes either of inferior vena caval or aortic homografts. The average per cent changes of the aortas and grafts in the different categories are listed as: (*A*), fresh inferior vena caval autografts (aortas 184+, grafts 198+), (*B*) delayed inferior vena caval autografts (aortas 97+, grafts 57+), (*C*) fresh inferior vena caval homografts (aortas 87+, grafts 12−), (*D*) delayed inferior vena caval homografts (aortas 106+, grafts 7−), (*E*) fresh aortic autografts (aortas 139+, grafts 141+), (*F*) fresh aortic homografts (aortas 167+, grafts 76+), (*G*) delayed aortic homografts preserved in light mineral oil (aortas 123+, grafts 60+), (*H*) delayed aortic homografts preserved in Ringer's solution (aortas 117+, grafts 52+), and (*I*) delayed aortic homografts preserved in Tyrode's solution (aortas 135+, grafts 51+).

that arterial grafts could be preserved for at least 6 months at 4° C. in light mineral oil and still be used successfully as vascular grafts. The reason for the decreased preservability of veins in mineral oil, as compared to arteries, is not clear. After about 2 months of such preservation, the veins became viscid in character, gray in color, and lost their tubular shape, becoming globular in outline when lifted up. Suturing of these grafts was practically impossible, although sutures once placed had no tendency to pull out.

Grafts kept in Ringer's or in Tyrode's solution, both containing 10 per cent homologous serum, were in a better state of preservation than were grafts kept in light mineral oil. However, while this difference was quite apparent in the case of vein grafts it was much less apparent in the case of arterial grafts. The graft preserved for 181 days (Fig. 10*A*) in mineral oil still had many stainable nuclei when implanted. Although the evidence is not conclusive, we suggest that the chief requirements of a satisfactory fluid medium for preserving vascular segments are that it should (A) keep the graft from dehydrating, (B) not alter the intracellular constituents of the graft cells, and (C) not increase the liability of the implanted graft to degenerative changes (as is the

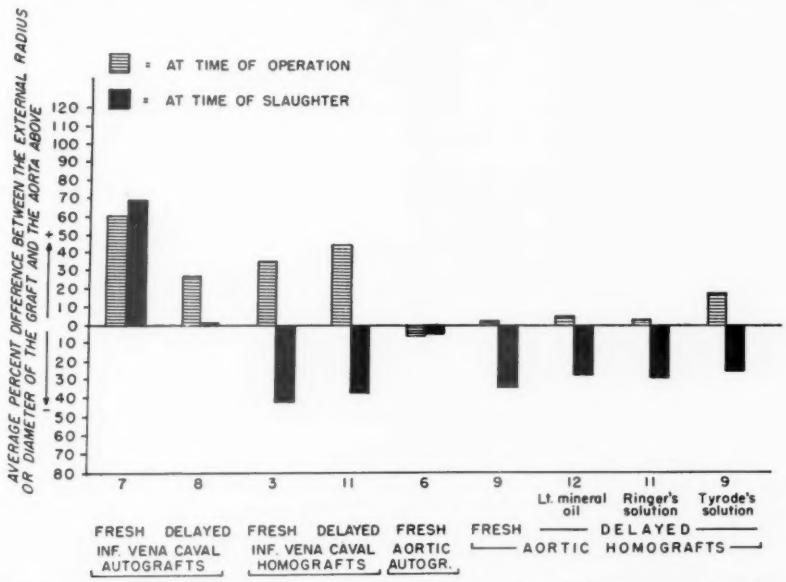


Fig. 22*B*.—Seventy-six vascular grafts implanted in the abdominal aortas of young pigs. (open at slaughter). Average per cent difference between the external radius or diameter of the graft and the aorta midway between graft and renal artery. Radius differences are averaged for the inferior vena caval autografts (both fresh and preserved), while diameter changes are averaged for the other types of grafts. The crosshatched columns represent the average difference at the time of operation, while the solid columns represent that at the time of slaughter. Columns below the zero line indicate that the graft average is smaller than the aortic average midway between graft and renal artery, above the line that the graft average is larger. The average per cent differences between the graft and aortic calibers at operation and at slaughter are listed as: (*A*) fresh inferior vena caval autografts (operation, graft 60 per cent larger; slaughter, graft 69 per cent larger), (*B*) delayed inferior vena caval autografts (operation, graft 26 per cent larger; slaughter, graft 1 per cent larger), (*C*) fresh inferior vena caval homografts (operation, graft 35 per cent larger; slaughter, graft 42 per cent smaller), (*D*) delayed inferior vena caval homografts (operation, graft 44 per cent larger; slaughter, graft 36 per cent smaller), (*E*) fresh aortic autografts (operation, graft 5 per cent smaller; slaughter, graft 4 per cent smaller), (*F*) fresh aortic homografts (operation, graft 3 per cent larger; slaughter, graft 33 per cent smaller), (*G*) delayed aortic homografts preserved in light mineral oil (operation, graft 6 per cent larger; slaughter, graft 27 per cent smaller), (*H*) delayed aortic homografts preserved in Ringer's solution (operation, graft 4 per cent larger; slaughter, graft 28 per cent smaller), and (*I*) delayed aortic homografts preserved in Tyrode's solution (operation, graft 18 per cent larger; slaughter, graft 24 per cent smaller).

case with formalin). It seems doubtful that these media function in a nutrient sense with respect to the grafts. Certainly, mineral oil would be incapable of such a function. However, it is probably of great importance that, if what is outside the cell is capable of passing through the cell membrane, it should resemble the normal intercellular fluid as closely as possible. On this basis, both hypotonic and hypertonic solutions would appear to be very poor preservative media. Accordingly, such balanced salt solutions as Tyrode's solution containing 10 per cent homologous serum or Ringer's solution containing 10 per cent homologous serum appear ideal, especially the former, with respect to their similarity to the intercellular fluid. A substance, as light mineral oil, which probably does not pass through the cell membranes would thus appear to maintain the cellular constituents within the cells in their original concentration. In essence, we suggest that if what is outside the cells is capable of osmotic interchange with the intracellular fluid it should resemble the normal intercellular fluid of the body as closely as possible. If what is outside the cells does not closely resemble the intercellular fluid, it should be of such character as not to be capable of osmotic interchange with the cells.

Vascular segments may be preserved at temperatures below 0° C. for prolonged periods and still be satisfactory for use as grafts. The biologic principles of such preservation are exceedingly interesting. Life and death at low temperatures have been shown by Luyet and Gehino (1940) to be determined by whether the low temperature preservation results in freezing or vitrification of the water content of the substance in question. Freezing refers to the solidification of water by a process which involves the rearranging of the molecular structure of water into the crystalline pattern of ice. Vitrification refers to the solidification of water by a process that does not alter its molecular structure.

The formation of ice crystals in tissue represents a severe form of tissue injury. One may hypothesize, with considerable basis, that the ice crystal formation results in the rearranging of the entire molecular architecture of the cells causing disruption of the cell membranes and death of the tissue as a consequence. Water can crystallize, i.e., freeze, only within a limited range of temperatures, 0° C. to –40° C. Below –40° C. freezing cannot occur. The speed at which a liquid freezes is called its crystallization velocity. Thus, if one can obtain a cooling velocity that is faster than the crystallization velocity of the water content of the substance in question, this substance can be vitrified. It is probably impossible to achieve a sufficiently rapid cooling velocity to vitrify vascular segments because the thickness of the vessel wall precludes sufficiently rapid cooling of the center of the wall to prevent its freezing. However, Luyet (1951) has shown that the size of small ice crystals increases tremendously if the temperature of the substance is brought up slowly through the temperature range –40° C. to 0° C. Thus, ice can form both going down and coming up through this critical temperature zone.

Encouraging results have been obtained by adhering to the criteria for minimal ice crystal formation, namely, rapid lowering of the graft temperature through the range of 0° C. to –40° C., storage at temperatures below –40° C., and rapid elevation of the graft temperature to above 0° C. just prior to use.

Eastcott and Hufnagel (1951) and Hufnagel and Eastcott (1951) have employed liquid nitrogen at –196° C. as the cooling medium with subsequent storage in a carbon dioxide ice refrigerator at –70° C. Their results have been excellent. Deterling, Coleman, and Parshley (1951) found cooling with carbon dioxide ice (–70° C.) to be a satisfactory means of lowering the temperature. Good results were obtained when the grafts were maintained below –40° C. during the storage period. Meeker and Gross (1951) observed comparable experimental findings using irradiated nonsterile grafts preserved at similarly low temperatures. They have used 2 such grafts successfully in patients with coarctation of the aorta. Hypertension was relieved in both instances. Swan, Feehan, Florio, and Johnson (1952) have reported promising results with arterial homografts quick frozen (carbon dioxide ice) in Ringer's solution containing 10 per cent homologous serum.

The feasible goal of low temperature preservation of blood vessel segments is preservation with minimal ice crystal formation. Such vessel segments may be kept for practically indefinite periods and still be used successfully as vascular grafts.

E. Suture Methods and Suture Types.—The function of the suture employed for vascular anastomoses is to maintain the edges of the vessels in contact in such a manner as to prevent hemorrhage, assure patency, and promote healing. Jassinowsky (1889) reported the first successful attempts at arterial anastomosis. He employed interrupted end-on coaptation stitches which excluded the intima, piercing only the media and adventitia. This method has found little favor. Crafoord (1947), using a continuous suture of this type, is one of the few to employ this intimal exclusion stitch. Silverberg (1899) reported the successful employment of a continuous end-on coaptation stitch including all layers for arterial anastomoses in dogs. Carrel (1902) added the feature of triangulation as a means of aiding the accurate placement of a continuous end-on coaptation stitch that included all layers. This method, with and without triangulation, is frequently used today. Jaboulay and Briau (1896) described the restoration of arterial continuity by interrupted everting mattress sutures. This method is used by Gross (1951), Shumacker (1951), and others. Clermont (1901) and Dorrance (1906) described the use of a continuous everting mattress suture for blood vessel anastomosis. This method is often used today, most notably by Blalock (1948). Nonsuture methods of blood vessel anastomosis (as described by Payr in 1900 and Blakemore, Lord, and Stefko in 1942) have largely been abandoned.

In our experience, we have found both the everting and end-on coaptation methods of vascular suture to be satisfactory. It is true that the end-on coaptation method is easier and quicker for the beginner than is the everting method. However, practice and experience enable one to perform an anastomosis by either method with comparable ease. The amount of suture material presenting within the lumen of the vessel is much greater with the end-on coaptation method than it is with the everting mattress method. In vessels of small caliber, this is probably a factor of importance relative to the incidence of thrombosis. By using very fine suture material, as 000000, and placing the

stitches very close to the vessel edge, both the presence and amount of intraluminal suture material can be greatly reduced.

We have shown (Sauvage and Harkins, 1952) that with growth of a vascular anastomosis performed with a fine continuous nonabsorbable suture, the suture first straightens and then pulls through the wall. If further growth occurs, the suture pulls in toward the lumen raising up a septum about the internal circumference of the vessel. If still further growth occurs, the septum becomes attenuated, then fenestrated, and finally disappears with restitution of the lumen as the suture is partially sequestrated into the lumen. The suture dangling in the lumen may act as a focus for thrombus formation. This sequence of events is true only if the continuous suture remains intact.

We showed that the tensile strength of 00000 silk decreases markedly after several months of implantation in the subcutaneous tissues of the dog (Sauvage and Harkins, 1952). The fact that only 1 of 105 continuous nonabsorable sutures employed in our study was broken at the time of slaughter does not mean that one should expect similar type sutures to remain intact in growing patients where the growth period extends over many years instead of a few months as in the pigs. We also showed (Sauvage and Harkins, 1952) that the end-on coaptation method requires more suture length than does the everting mattress method. Thus, when the continuous end-on coaptation method is employed more growth can occur before the suture straightens than when the everting mattress method is used. In addition, the amount of suture needed for the anastomosis is increased by placing the stitches farther back from the vessel edge with the end-on coaptation method but not with the everting mattress method. Otherwise, the sequence of events is the same for anastomoses performed with continuous fine nonabsorbale sutures by either of these two methods. There is no limitation of anastomotic growth when a continuous catgut suture is employed or if one-half of a nonabsorbable suture line is interrupted regardless of the suture method (Fig. 2).

It would seem that the suture method employed for any anastomosis should be the type with which the surgeon has the greatest degree of proficiency and which appears to be best suited to the peculiarities of the situation in question. When growth is a factor, interruption of the nonabsorbable suture line anteriorly would seem to be a wise precaution.

F. Relation of Graft Complications to Graft Length.—Swan recently stated (1952) that "it is possible that the length of graft which can be safely used may prove to be a function of its diameter." This appears to be a sound appraisal of the situation. The larger the caliber of a vessel, the longer the length that can be used successfully as a graft. Occlusive thrombosis occurs rarely in large arteries, as the aorta, but frequently in small ones. McCune and Blades (1951), on the basis of experiments in which they studied canine aortic homografts up to 22 cm. in length, stated that they believed "that the viability of preserved blood vessel grafts is not related to length." Anzola, Palmer, and Welch (1952), from experiments with long femoral and iliofemoral arterial homografts (8 to 38 cm. in length) in dogs, observed that such grafts functioned for only short periods of time (4 weeks) at which the majority showed evidence of throm-

bosis. In all instances, the site of this delayed thrombosis was toward the center of the graft rather than at the suture line. Differing from the arterial homografts, long-length fresh venous autografts implanted in the same portion of the arterial tree in other dogs did not show this high incidence of delayed thrombosis.

It seems reasonable to assume that the longer the length of homograft to be replaced by the host, the greater would be the liability to graft complications, especially thrombosis (delayed), stenosis, and degenerative change. Also, it appears safe to conclude that if short-length grafts of a certain type do poorly, longer length grafts of this same type would do no better. However, the fact that short-length grafts of a certain type do fairly well does not mean that longer length grafts of this same type would do equally as well. Fresh arterial autografts would appear to be an exception to this generalization since they maintain their cellular integrity and are not replaced by the host.

It is probable that the already high incidence of dilatation occurring in short-length fresh inferior vena caval autografts implanted in the abdominal aorta of the growing pig would be higher in longer length grafts of this same type implanted in the same area. Similarly, the poor results (mainly stenosis) obtained with short-length inferior vena caval homografts, fresh or preserved, would probably be worse with longer length grafts of this same type. It is impossible to say whether or not longer length arterial homografts, fresh or preserved, would give as high a percentage of partially satisfactory results in the aorta of the growing pig as the short-length grafts reported in this paper. The answer to this problem is extremely important. There may be such a high incidence of degenerative change and stenosis in long-length arterial homografts that their use would be ill advised in growing patients in all but the most desperate of circumstances. Such possibilities are only conjecture at this time and must await the results of further experimentation for confirmation or denial.

G. Advantages and Disadvantages of Various Types of Vascular Grafts.—There is only one type of graft implanted in the arterial system that may be relied upon to give uniformly satisfactory results (Table III and Fig. 2). This is the fresh arterial autograft. These grafts maintain their cellular integrity and resemble the adjacent artery in all obvious respects both grossly and microscopically. This is the ideal graft for use in the arterial system. It is unfortunate that practically all parts of the arterial system are indispensable. It would be most desirable, especially in children, to employ fresh arterial autografts to bridge the defect in those cases of coarctation of the aorta where grafts are necessary to restore normal continuity of the aorta. Shumacker (1951) has employed the left subclavian artery as a free graft to restore aortic continuity in certain cases of coarctation. Hurwitt and Kantrowitz (1952) have spliced segments of the splenic artery together and used the resultant patchwork graft successfully in the abdominal aortas of dogs. Schmitz, Kiriluk, Hoag, Kanar, Sauvage, Harkins, and Merendino (1952) have made "compilation" arterial autografts and used them successfully to bridge short

defects in the thoracic aortas of dogs. The obvious limitation of this method is that these grafts are of short length. However, the principle appears sound and in suitable cases this type of graft should give satisfactory results.

Fresh venous autografts implanted in the arterial system thicken but never come to resemble the normal cellular architecture of arteries. For bridging defects in arteries smaller in size than the thoracic and abdominal aorta, fresh venous autografts can be safely procured and successfully employed in many instances. For vessels of this size, venous autografts have the advantages of availability and autogenicity. These grafts have a very low incidence of degenerative change. The venous system is well adapted to serve as an autogenous donor. Practically any superficial vein, both saphenous and superficial femoral veins, both external jugular veins, one internal jugular vein, the azygos vein, and others may be removed without serious risk to the patient. There is, then, no need to preserve venous grafts. However, it is unlikely that unsupported venous autografts will find extensive application in the reparative surgery of the aorta, especially the thoracic, because of the necessity for a large caliber graft and the dangers incumbent upon resecting autogenous veins of the necessary size.

Also, dilatation of fresh autogenous vein grafts implanted in the arterial system appears to be related to the extent of surrounding and supporting tissues. Dilatation of such grafts is pronounced in the thoracic aorta as shown by Sako (1951), Johnson, Kirby, and Hardy (1953), and Schmitz, Sauvage, Kanar, and Harkins (1952). Dilatation is less constant in the abdominal aorta. The reaction of these grafts in the abdominal aorta of the growing pig is variable (Figs. 11 and 12). However, it may be possible to circumvent the dangers associated with the procurement and use of large caliber venous autografts in the aorta. Sako (1951) has shown that both fascia lata and cutis grafts applied as jackets about fresh venous autografts implanted in the thoracic aortas of dogs will prevent dilatation of these grafts. Our group is investigating the influence of such supporting jackets, as well as the effect of dicetyl phosphate upon the dimensional changes of fresh venous autografts implanted in the aortas of young pigs. In addition, studies are being formulated relative to the feasibility and practicality of taking veins of a size that can be safely resected and by a process of "compilation" making a composite graft of adequate size for the thoracic aorta.

The hypothesis that from small veins one could make a large caliber graft which, when properly supported, would not undergo dilatation is most attractive. Such grafts would have the dual advantages of availability and autogenicity. However, this is but a working hypothesis and must await the results of further experimental trial before a decision as to its merits can be reached. In the periphery where there is heavy *musculofascial* support, dilatation appears not to be a problem, either experimentally (Anzola, 1952) or clinically (Murray, 1952). Schmitz, Kanar, Sauvage, Storer, and Harkins (1953) have demonstrated that subsequent dilatation of fresh venous autografts implanted in the aortas of both mature dogs and growing pigs is not related to the graft-aortic diameter ratio at time of implantation. Thus, in

areas with little surrounding and supporting tissue fresh venous autografts will dilate even though they are well matched with respect to the caliber of the recipient artery.

Delayed venous autografts probably have a low incidence of degenerative change and are not as subject to dilatation as fresh venous grafts. However, in those areas of the arterial circuit where veins of the caliber that can be safely procured are used dilatation is not a problem. Thus, the clinical use of delayed venous autografts would appear to be limited.

Arterial homografts have the disadvantages of difficulties in procurement, necessity of storage, liability to degenerative change, and decreased rate of growth as compared to the aorta of the growing pig (Fig. 22*A*). They have the advantage that they may be used to bridge long aortic defects. The use of these grafts is the safest and most practical method available for bridging such defects. Gross (1951), Lam (1951), Oudot (1951), Schafer and Hardin (1952), Dubost, Allary, and Oeconomos (1952), and Murray (1952) have all reported the successful employment of arterial homografts in the aorta. However, the risk associated with the use of long-length aortic homografts in children cannot yet be calculated because of insufficient experimental evidence.

Venous homografts would seem to have little place in the reparative surgery of the arterial system. They have the same disadvantages of difficulty in procurement and necessity of storage as arterial homografts. Their liability to rupture is much greater than arterial homografts. Their susceptibility to degenerative changes (Fig. 14) is no less than that of arteries. Their tendency toward stenosis in the abdominal aorta of the growing pig is much more pronounced (Figs. 15, 16, and 22*A*) than is the case with arterial homografts. Thus, whenever venous homografts could be used, arterial homografts could be used better.

In the venous system, there is only one type of graft to use and that is the fresh venous autograft. Southwick (1951) and Gerbode (1951) have shown that arterial homografts implanted in the venous system become occluded. It is probable that the intraluminal venous pressure is not sufficient to counteract the inherent tendency of the fibrous tissue of the "replaced" graft to contract. In the arterial system, the high intraluminal pressure acts as an effective dilator in most cases. Southwick (1951) demonstrated that fresh venous autografts in the venous system remain patent. Such grafts have been used successfully in treating patients with portal hypertension by Reynolds and Southwick (1951), Blakemore and Fitzpatrick (1951), and Rousselot (1952).

SUMMARY

The results obtained with several different series of vascular grafts implanted in the abdominal aortas of 148 young pigs have been presented. These results have been analyzed and comparisons made between the different types of grafts—autogenous and homogenous, fresh and preserved, arterial and venous. Emphasis has been placed on the occurrence of the graft complications of thrombosis, rupture, dilatation, stenosis, and degenerative change.

The use of light mineral oil as a preservative medium for vascular grafts has been described. Suture types and suture methods have been analyzed with respect to their relation to subsequent anastomotic growth. Several important aspects relative to types, means of preservation, and methods of suture of vascular grafts have been discussed.

CONCLUSIONS

1. Fresh aortic autografts of the abdominal aorta of the growing pig maintain their cellular integrity and give satisfactory results.

2. In the majority of instances, short-length arterial homografts, whether fresh or preserved, give results that are partially satisfactory when implanted in the abdominal aorta of the growing pig. Preservation of cellular integrity of such grafts, presumably viable at implantation, is most unusual, and the conditions of this exceptional occurrence have not been adequately defined.

3. Fresh inferior vena caval autografts implanted in the abdominal aorta of the growing pig tend to be variable in their dimensional changes. Dilatation frequently occurs.

4. In the majority of instances, delayed inferior vena caval autografts implanted in the abdominal aorta of the growing pig tend to increase in dimensions but at a slower rate than does the aorta of the host.

5. In many instances, inferior vena caval homografts of short length, whether fresh or preserved, when implanted in the abdominal aorta of the growing pig give results that are unsatisfactory because of stenosis.

6. Light mineral oil can be used successfully as a medium for preserving arteries for long periods at temperatures slightly above 0° C. However, veins are poorly preserved by this method.

7. Both Ringer's solution plus 10 per cent homologous serum and Tyrode's solution plus 10 per cent homologous serum appear to be superior to light mineral oil as preservative media for vascular segments, especially veins. However, the appearance of the graft after several months of implantation in the abdominal aorta of the growing pig gives no clue either as to the duration of the period of preservation prior to implantation or as to which of these media was used for storage of the graft.

8. The development of degenerative changes (calcification or atheromatous plaque formation) in vascular homografts may be the result of a specific host-graft reaction that is not greatly augmented by increasing the period of preservation of the graft by the methods employed in this study at least for periods up to 6 months prior to implantation.

9. The end-on coaptation method of vascular suture has the advantage of being quicker and easier than the everting mattress method, but with experience this becomes a matter of minor importance. The end-on coaptation method has the disadvantage of placing considerable suture within the lumen of the vessel. This factor is minimized by placing the stitches close to the vessel edge.

10. Size 00000 catgut is satisfactory for use as a vascular suture. Anastomoses performed with continuous catgut show no constriction with growth of the vessel.

11. Interruption of approximately one-half of a nonabsorable suture line will provide for unimpeded growth of the anastomosis. It is not important from the growth aspect whether these interrupted stitches be of the end-on coaptation or everting mattress types.

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The Physiologic Effects of Wounds. By The Board for the Study of the Severely Wounded, North African-Mediterranean Theater of Operations. Published by the Office of the Surgeon-General, Department of the Army, Washington, D. C., 1952.

This work is a compilation of physiologic studies of the wounded man in battle performed during World War II in the North African-Mediterranean theaters by a special study board organized for this primary purpose.

As a result of these observations, certain concepts concerning shock, its pathogenesis, and its management have been clarified. Based on a study of 186 wounded men, the findings show that severe hemoconcentration does not occur under battle conditions except following special types of injury such as burns, crush syndrome, and certain abdominal wounds. In fact, it was pointed out that associated with wounding and hemorrhage, the hematocrit value fell rapidly. The plasma protein level, however, decreased only a small amount, in general only about one-fourth as much as the hematocrit. This observation implies that the hemodilution which characteristically follows hemorrhage and shock occurs by means of a protein-rich diluent. It was shown that men can lose up to 75 per cent of their blood volume and yet recover, which is more than has generally been supposed. Furthermore, it was pointed out that there is in general a quantitative relationship between the loss of blood volume and the degree of shock. These observations support the view that the major cause of shock is hemorrhage.

Detailed biochemical examinations of other organ systems offer evidence of abnormal function to a greater or lesser degree in all instances. With regard to the kidney, depression of glomerular filtration, renal plasma flow, and tubular excretion were observed somewhat in proportion to the degree of early shock. Lower nephron nephrosis is elaborated upon with documentation from the point of view of diagnosis, biochemical changes, pathology, and treatment. Impairment of liver function was observed following wounding, as evidenced by an average bromsulfalein retention of 12.4 per cent in fifty-nine patients.

The studies presented in this volume and the concept which fostered them have created a milestone in military surgery in that they represent the first organized effort to secure information concerning battle injuries in a scientific manner on, or adjacent to, the battlefield. In this instance, the research laboratory has been brought to the patient, and a detailed study of a clinical problem carried out. It is the opinion of this reviewer that these studies fulfill the promise inherent in clinical investigation, that is, the answer to a clinical problem. The importance of this concept is attested to throughout our university teaching hospitals by their associated clinical investigation groups. The value of the data contained in this volume supports the importance of this concept, and should foster the development of such investigative teams as an integral part of the armed forces.

Of special note is the introductory chapter which outlines the background to the shock problem, shows the difficulties encountered in the management of the severely wounded during World War II, and tells how these problems were met. This book is recommended as required reading for every surgeon.

Brain Surgeon. By William Sharpe, M.D. Pp. 266. New York, 1952, Viking Press, Inc., $3.75.

This book is the autobiography of an apparently successful physician. In a comprehensive account of his life's experience, Dr. Sharpe tells of his college and medical-school days at Harvard, of his training in neurological surgery at Johns Hopkins Hospital under the famous Dr. Cushing, and of his experiences in the practice of surgery in China and later in New York City. In traveling still more extensively, Dr. Sharpe met Hitler, then Stalin. These uncommon experiences add interest to the book, as do the author's recollections of his colorful relationships with his medical colleagues.

With firm conviction, Dr. Sharpe discusses medical practice as he experienced it. Much of this was during the relatively early development of neurosurgery. Particular emphasis is given the fundamental surgical problems of head injury and cerebral palsy. Indeed, the general public, to whom the sale of this book seems to be at least partially directed, may possibly fail to detect within its pages the importance of the temporal element in medical progress.

There is no doubt that this book conveys the personality of Dr. Sharpe. That alone is sufficient reason to recommend it.

The Battle for Mental Health. By James Clark Moloney, M.D. Pp. 105. New York, 1952, Philosophical Library, Inc. $3.50.

This little volume is written ostensibly to impress the layman with the enormous problem of mental ill-health and to suggest methods of prevention. In both purposes it seems to have failed.

The author, who is announced by the publishers as an eminent American psychoanalyst, is a member of the Cornelian Corner group in Detroit. This volume is presented as an exposition of the doctrines and beliefs of this group. Most of the mental ills of the present day he attributes to harmful influences of the first few days of life. By inference, the reader is led to believe that if the newborn were left with the mother rather than kept in a nursery, most of the mental disturbances of later life would be avoided.

The reviewer, who is not a psychiatrist, finds the book strangely unconvincing even though the publishers claim that "Dr. Moloney supports his theories with scientific clinical, anthropological and experimental observations." The reader will search in vain for factually supported data. Rather will he find sweeping generalizations. The bottle-fed baby is portrayed as having "had no warm, interpersonal relationship with his mother" at the head end, yet "at the other end . . . a warm relationship . . . for it was customary for her to cleanse the baby's buttocks with one hand as she held the baby's feet up with the other hand. . . . Therefore, at the buttocks, genital or anal end, a type of direct experience with the mother took place which had no counterpart at the mouth or head-end" with the result that "the baby subsequently surrendered the mouth end of his body as a site for love in favor of the anal end which was more considerately treated." One wonders if Dr. Moloney ever saw a mother kiss a baby on the head or neck.

His attack on obstetrical practices is ill tempered and emotional. The reviewer cannot agree that obstetricians, pediatricians, and maternity nurses are motivated by "their inner needs to secure these roles for neurotic self-fulfillment," that "efficient, childless women as supervisors dominate nurseries" or that obstetricians are "intellectual stop-cocks to social progress" who through their "unconscious conspiracy with maternity and hospital nurses, their unconscious collusion with hospital management" have "undermined the gains made in the field of infant mortality and maternal mortality."

Emotional outbursts of this type are not designed to convince the lay reader of the critical judgment of the author or the soundness of the doctrines that he preaches. It is unfortunate that a problem so important for society and a new approach so potentially helpful does not find a more temperate and convincing champion.

Intracranial Aneurysms. By Wallace B. Hamby, M.D. Pp. 564. Springfield, Ill., 1952, Charles C Thomas, Publisher. $14.25.

Dr. Hamby's purpose in writing this book was to assemble in one volume the known data on intracranial aneurysms. Where it was not possible to reiterate all such data, he has offered an extensive bibliography. Each of the seven chapters is an entity. This makes unavoidable repetition of some of the material, but increases the value of the book for reference use since a complete discussion of a problem is to be found all in one place.

The first chapter is a review of the anatomy and a discussion of the physiology of cerebral circulation. Methods and effects of ligation of the carotid and vertebral vessels make up a considerable part of this section. Complications of ligation are included. The second chapter is a discussion of the incidence and location as well as a description of the various types of aneurysms. This is mainly a review of the literature and in parts is rather indefinite. The third chapter concerns the diagnosis of anuerysms. This includes symptomatology as well as diagnostic procedures of ventriculography, pneumoencephalography, and arteriography. The discussion of the latter is excellent. Although many of the photographs are not clear, the accompanying drawings make possible ready interpretation.

The last four chapters comprise the major portion of the book and are devoted entirely to the surgery of intracranial aneurysms. The author, a practical surgeon, in these last chapters utilizes illustrative cases from his extensive experience, and, in general, the style and diction of this part of the book are more clear and interesting. He discusses the treatment of ruptured as distinct from unruptured aneurysms. He has included a short section on general surgical principles as they apply to the surgery of aneurysms.

This is a valuable monograph which should have lasting value. It is a well-documented complete treatise on intracranial aneurysms useful for reference by specialists in neurology and neurologic surgery.

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- Steraject Penicillin G Procaine Crystalline in Aqueous Suspension (300,000 units) (600,000 units) (1,000,000 units)
- Steraject Permapen* Aqueous Suspension (dibenzylethylenediamine dipenicillin G) (600,000 units)
- Steraject Combiotic® Aqueous Suspension (400,000 units Penicillin G Procaine Crystalline, 0.5 Gm. Dihydrostreptomycin)
- Steraject Dihydrostreptomycin Sulfate Solution (1 Gm.)
- Steraject Streptomycin Sulfate Solution (1 Gm.)

Pfizer

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*TRADEMARK, CHAS. PFIZER & CO., INC.